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Preparation of enantiopure biimidazoline ligands and their use in asymmetric catalysis

Nicola A. Boland, Mike Casey,* Stephen J. Hynes, Jonathan W. Matthews, Helge Müller-Bunz and Philippa Wilkes

Chemistry Department, the Centre for Synthesis and Chemical Biology, the Conway Institute of Biomolecular and Biomedical Research, University College Dublin, Dublin 4, Ireland. E-mail: mike.casey@ucd.ie; Fax: +353 1 716 2127; Tel: +353 1 716 2420

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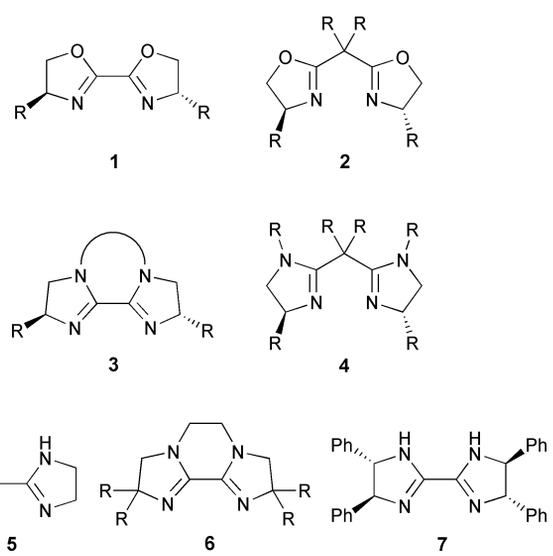
A convenient new method for the preparation of 2,2′-biimidazolines is reported. Amino alcohols were reacted with dimethyl oxalate, and the product hydroxy amides converted into chloroamides by reaction with thionyl chloride. Treatment with PCl_5, followed by diamines (ethanediamine, propane-1,3-diamine, 2,2-dimethylpropane-1,3-diamine) furnished a series of enantiopure tricyclic biimidazolines. Complexes of two of the ligands with $PdCl_2$ were prepared and their X-ray crystal structures were determined. The biimidazolines were tested as ligands for asymmetric Pd-catalysed allylations. Moderate enantioselectivity (up to 80% ee) was found for the reaction of dimethyl malonate with diphenylallyl acetate, with the 5,7,5 fused tricyclic systems outperforming the 5,6,5 analogues. The corresponding reaction of pentenyl acetate gave lower enantioselectivity (44–57% ee), and proved very sensitive to the donor strength of the ligands, the stronger donors giving lower yields. The results provide a further demonstration of the value of the 'tunability' of imidazoline ligands.

Introduction

In the course of the explosive development of the field of asymmetric catalysis over the last 15 years, some ligand structures have emerged as being particularly useful. The oxazolines are one such highly successful ligand family, and C_2 symmetric bisoxazolines such as **1** and **2** are very widely used.[1] 2,2′-Bioxazolines **1** are among the best available ligands for several transition metal-catalysed reactions, including Rh-catalysed hydrosilylation of acetophenone,[2] Pd-catalysed cyclisation–hydrosilylation of dienes,[3] and Pd-catalysed bis-(alkoxycarbonylation) of alkenes.[4]

We became interested in the use of tricyclic biimidazolines **3** as conformationally restricted analogues of bioxazoline ligands. We hoped that they would be useful alternatives to the bioxazolines because the conformational rigidity and greater donor strength (being amidines, they are much more basic than oxazolines[4]) would promote metal coordination. We also anticipated that variation of the tether linking the two nitrogen atoms would allow tuning of the properties of the ligands. This study is part of a larger effort to determine if the extra 'tunability' arising from the presence of an additional substituent in chiral imidazoline ligands, such as **3** and bisimidazolines **4**, will confer an advantage over analogous oxazolines. We,[6] along with Busacca *et al.*[7] and Pfaltz *et al.*,[8] have begun to explore the use of imidazoline ligands[9] as alternatives to oxazolines, with very promising results. In addition to their potential for use as chiral ligands in a range of metal-catalysed reactions, we hoped that the biimidazolines **3** might also prove useful as precursors for chiral cyclens[10] and chiral carbenes.[11]

In contrast to bioxazolines, biimidazolines have received very little attention. The coordination chemistry of the parent 2,2′-biimidazoline **5** has been studied,[12] and some of its complexes have been investigated as enzyme mimics.[13] Several tricyclic derivatives of **6** have been prepared by Weisman and co-workers and their coordination chemistry has been explored.[10,14] Chiral biimidazoline derivatives have scarcely been studied. Dupont *et al.* prepared one example, **7**, by the condensation of stilbene diamine with an oxalimidate,[15] and Müller synthesised several others, again using diamine (or tetraamine) condensation reactions.[16] The products were used as ligands for asymmetric catalysis with moderate success.



We now report a simple new method for the preparation of a series of enantiopure 2,2′-biimidazolines, **3**. We also report preliminary results showing that they are viable ligands for asymmetric catalysis, and that their reactivity profile in Pd-catalysed allylation reactions experiments is quite different to the corresponding bioxazolines.

Results and discussion

Preparation of biimidazolines

Biimidazolines have invariably been prepared from diamines (or tetraamines).[17] Because of the relative difficulty of obtaining suitably substituted enantiopure diamines, we sought to apply our new imidazoline synthesis,[18] which begins from amino alcohols, and allows easy variation of the N-1 substituent. Following literature procedures,[2,19] enantiopure amino alcohols were condensed with dimethyl oxalate to give the bishydroxy-amide **8** compounds, which were chlorinated with thionyl chloride to furnish the corresponding chlorides, **9** (Scheme 1). These compounds are familiar as precursors for bioxazolines.[19]

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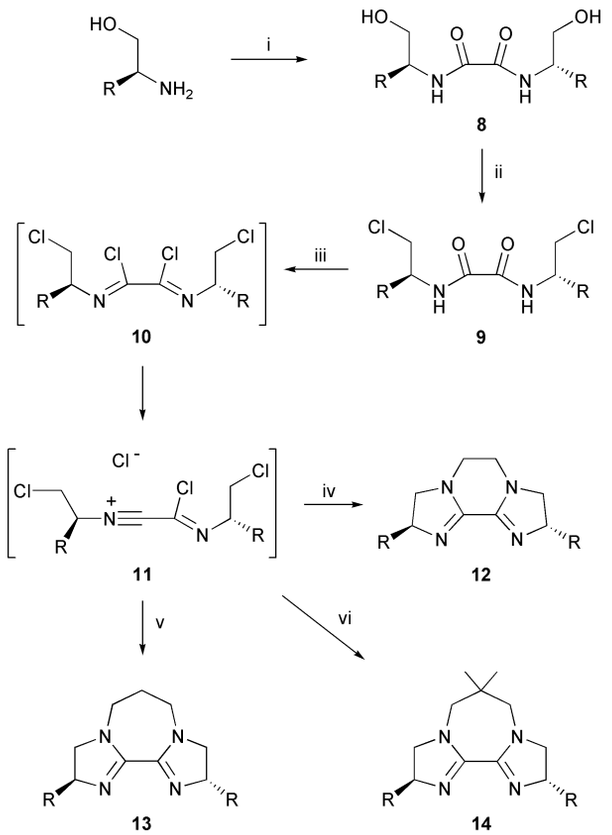


Scheme 1 *Reagents and conditions:* i, $(CO_2Me)_2$, toluene, reflux; ii, $SOCl_2$, toluene, 90 °C; iii, PCl_5, toluene, 85 °C; iv, $(CH_2NH_2)_2$, Et_3N, CH_3CN, reflux; v, $CH_2(CH_2NH_2)_2$, Et_3N, CH_3CN, reflux; vi, $CMe_2(CH_2NH_2)_2$, Et_3N, CH_3CN, reflux.

Reaction with PCl_5 in toluene at 85 °C, until evolution of HCl ceased, cleanly gave the oxalimidoyl chloride **10** compounds,[20] which could be characterised by ^{13}C NMR spectroscopy ($\delta_{C=N}$ approx. 140 ppm).

The imidoyl chlorides (**10**) were expected to provide imidazolines by double nucleophilic substitution of the chlorides by amines. However, they proved quite resistant to substitution, possibly because formation of the nitrilium ion intermediates (*e.g.* **11**), which is rate determining,[21] is disfavoured by inductive effects. Indeed, imidoyl chlorides were sometimes isolated unchanged from attempted reactions with diamines, even after workup with aqueous hydroxide. After some experimentation, it was found that use of acetonitrile as the solvent for the substitution reactions gave the best results (Scheme 1, Table 1), presumably by promoting nitrilium ion formation.[22] Imidoyl chloride formation could also be achieved in acetonitrile, but it was better to carry out that step in toluene, and then to remove the solvent and phosphorus oxychloride, and carry out the diamine condensation in acetonitrile in the presence of an excess of triethylamine.

Reaction with 3 equivalents of ethylenediamine gave the 5,6,5 fused biimidazoline **12** compounds in good yields after purification by chromatography and crystallisation. Formation of 5,7,5 analogues (**13**) using propylenediamine proved considerably more difficult, partly because the cyclisations to form 7-membered rings did not proceed so cleanly, and partly because the products were much more polar than the 6-ring analogues (**12**), and were correspondingly more difficult to purify by chromatography. We reasoned that both of these problems might be ameliorated by the use of 2,2-dimethylpropane-1,3-diamine to prepare derivatives of **14**. These hopes were partly realised, in that the crude products were cleaner and easier to purify, but the yields of the pure **14** biimidazolines were not greatly improved (Table 1). Although the yields of the 5,7,5 products were poor, the brevity of the synthetic route means that hundreds of milligrams of these ligands can easily be obtained.

Table 1 Yields (%) of biimidazolines from amino alcohols

R	8	9	12	13	14
Bu^i, **a**	86	98	66		40
Pr^i, **b**	87	97	70	30	45
Bn, **c**	89	86	63	30	

It can be seen from Table 1 that several amino alcohols have been used, so this method is adaptable to the preparation of a wide range of biimidazolines. One restriction is that the phenylglycinol-derived oxalimidoyl chloride (**10**, R = Ph) gave substantial amounts of an unidentified side product, and the product biimidazolines were obtained in poor yields and could not be purified sufficiently to permit characterisation.

The new route is short and uses simple reagents, and we believe that it offers significant advantages in ease and versatility over strategies based on the use of enantiopure diamines. Most of the biimidazolines were obtained as crystalline materials, and all could be stored for prolonged periods without taking special precautions to prevent hydrolysis.[23]

Two other variations in the tether between the nitrogen atoms were investigated. Condensation of the valine-derived bisimidoyl chloride with *ortho*-phenylenediamine did give the expected biimidazoline **15**, but it proved very difficult to purify and the best yield, after repeated chromatography, was 25% of slightly impure material. Further work will be required to develop purification procedures for these tetracyclic derivatives. Reaction of the leucine derived bisimidoyl chloride with racemic stilbenediamine gave a 1 : 1 mixture of diastereomeric biimidazolines **16a** and **16b**.[24] The diastereomers was separated by chromatography, though **16a** was not obtained analytically pure, and their stereochemistry was established by NOESY experiments. The most useful NOE correlations are shown in Fig. 1 and they are fully in accord with the stereochemical assignments. The presence of strong NOE correlations between the *ortho* hydrogens and H-2 in **16a**, and between the *ortho* hydrogens and the isobutyl hydrogens in **16b** indicated that conformations in which the phenyl groups are pseudoaxial are important in both isomers.

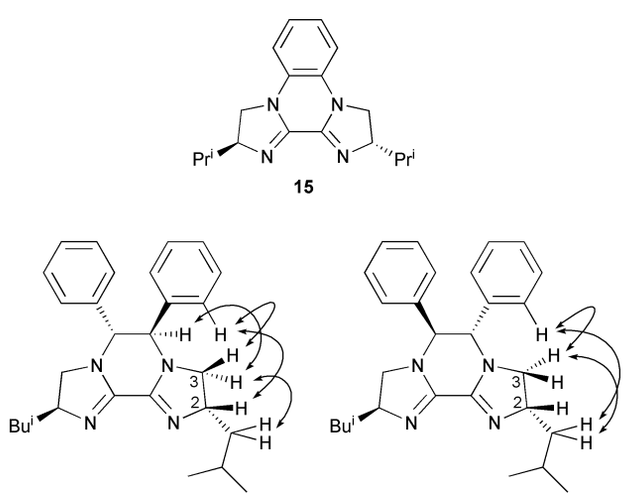


Fig. 1 Diagnostic correlations observed in the NOESY spectra of biimidazolines **16a** and **16b**.

Crystal structure determination of the $PdCl_2$ complexes of ligands 12b and 14b

Because the biimidazolines were used as chiral ligands in a Pd-catalysed reaction (see below), we hoped that useful information could be obtained by carrying out X-ray crystal structure determinations of model palladium complexes. Reaction of

biimidazolines **12b** and **14b** with $(PhCN)_2PdCl_2$ in methanol gave stable complexes **17** and **18**, and slow evaporation of solutions, in acetonitrile and dichloromethane, respectively, yielded crystals of both complexes suitable for X-ray diffraction.

Two independent molecules of complex **17** were present in the unit cell, each of which had the expected square planar geometry. One molecule is depicted in Fig. 2 and it may be seen that the ligand is essentially planar, as expected, with shallow puckering of the imidazoline rings and the central ring assuming a half-chair conformation, with some pyramidalisation at the two nitrogens. The mean ligand plane is tilted slightly relative to the plane containing the Pd and two Cl atoms (Fig. 3). The second molecule in the unit cell is very similar to the first, the chief difference being that the angle between the mean ligand plane and the coordination plane of the Pd is slightly different (Fig. 3). The structure of the ligand in the two complexes is very similar to that found in crystal structures of complexes of the unsubstituted analogue (**6**, R = H).[10a,14]

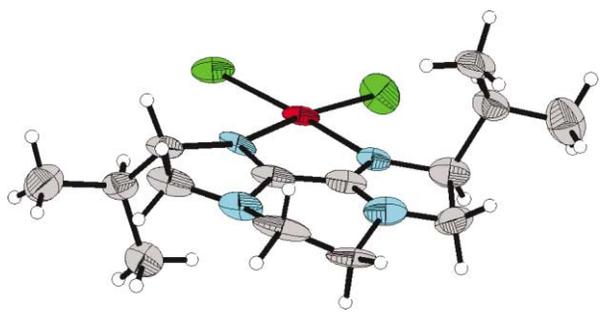


Fig. 2 X-ray crystal structure of one molecule of complex **17**, thermal ellipsoids are drawn on the 80% probability level.

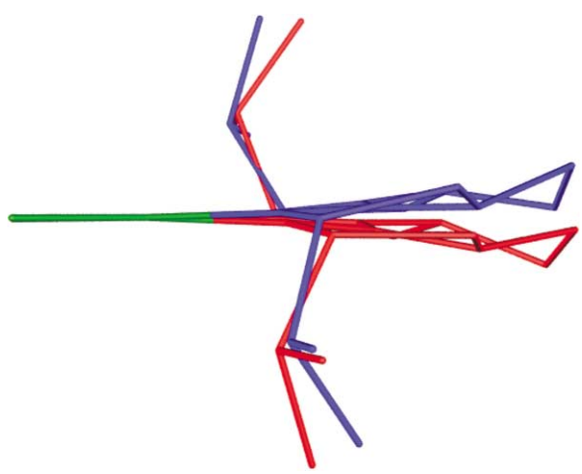
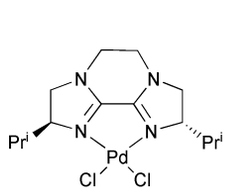
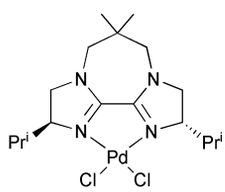


Fig. 3 Side view of a superimposition of the two molecules of complex **17** (blue and red), obtained by superimposition of the Pd and two Cl atoms (green). Hydrogens are omitted for clarity.



17



18

The crystal structure of complex **18** revealed that the unit cell contained two symmetry related molecules of a simple square planar complex (Fig. 4), along with two solvent molecules. The biimidazoline core of the ligand again is almost planar, and the central 7-membered ring adopts an 'envelope' conformation,

Table 2 Selected bond lengths [Å] and angles [°] for complexes **17**, **18** and **19**

	Complex **17**[a]	Complex **18**	Complex **19**[b]
Pd–N(1)	2.067(6), 2.041(8)	2.012(3)	2.003(2)
Pd–N(2)	2.051(6), 2.060(7)	2.019(2)	2.009(2)
Pd–Cl(1)	2.2819(19), 2.296(2)	2.2967(8)	2.2854(7)
Pd–Cl(2)	2.291(2), 2.285(2)	2.2905(8)	2.3080(7)
N(1)–Pd–N(2)	81.8(3), 82.5(3)	79.19(12)	79.42(9)
ψ_1	120.0(7), 118.7(8)	115.2(3)	114.4(2)
ψ_2	118.9(7), 118.2(8)	114.8(3)	114.8(2)
θ_1	121.2(7), 121.5(9)	127.9(3)	129.7(2)
θ_2	122.0(7), 121.4(8)	128.6(3)	128.7(2)

[a] Values for the two independent molecules. [b] Ref. 15.

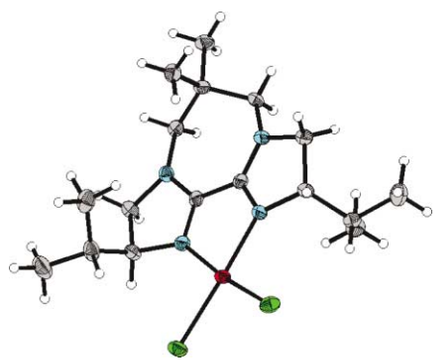
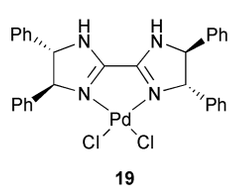


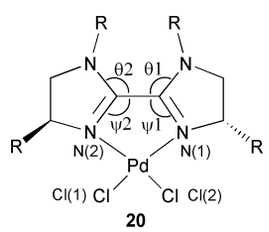
Fig. 4 X-ray crystal structure of complex **18**, thermal ellipsoids are drawn on the 50% probability level.

with slight pyramidalisation at the two imidazoline nitrogens contained within the ring.

Some key bond lengths and angles for complexes **17** and **18** are listed in Table 2, along with the corresponding values for complex **19**, reported by Dupont *et al.*[15] To facilitate comparisons, the atoms and bond angles in the three structures are labelled as shown in structure **20**. The bond lengths and angles within the organic ligands are unexceptional. The Pd–Cl bond lengths in all three complexes are very similar, but the Pd–N bonds are significantly longer in complex **17** than in the others.



19



20

Complex **17** also differs substantially from the others in the bond angles around the central ring. The angles θ_1 and θ_2 are close to 121° in **17**, but they are significantly larger in **18**, as would be expected for a seven-membered ring. As a consequence of this increase, the angles ψ_1 and ψ_2 are approximately 4° smaller in the 5,7,5 complex **18** than in the 5,6,5 analogue **17**. Thus, changing the size of the central ring has the effect of tuning the bite angle of the ligands, albeit only to a small extent. This effect is clearly visible in the superimposition of the structures shown in Fig. 5. Only one of the molecules of complex **17** is depicted because the relevant structural features in the second are almost identical.

A view of the superimposed complexes along the coordination plane of the Pd shows another significant difference (Fig. 6). Differences in the puckering of the imidazoline rings cause the isopropyl groups to be oriented at a significantly higher angle relative to the square plane in the 5,7,5 system **18** than in the 5,6,5 analogue **17**.

Table 3 Asymmetric allylation reactions

Ligand	22a		22b	
	Yield (%)[a]	Ee (config) (%)[b]	Yield (%)[a]	Ee (config) (%)[c]
12a	97	60 (*S*)	42	51 (*S*)
12b	88	55 (*S*)	50	56 (*S*)
12c	52	45 (*S*)	42	44 (*S*)
13b	76	76 (*S*)	33	57 (*S*)
13c	89	58 (*S*)	11	45 (*S*)
14a	97	80 (*S*)	21	Nd
14b	55	72 (*S*)	17	Nd
16a	56	57 (*S*)		
16b	73	57 (*S*)		
1a	86	77 (*S*)		

[a] Yields were determined by integration of the ^{1}H NMR spectra of the crude products, using naphthalene as an internal standard. [b] Ee values determined by HPLC using a Chiralcel OD H column, and configurations were assigned by polarimetry, ref. 19(*b*). [c] Ee values determined by ^{1}H NMR using Eu(hfc)$_3$, and configurations were assigned by polarimetry, ref. 28.

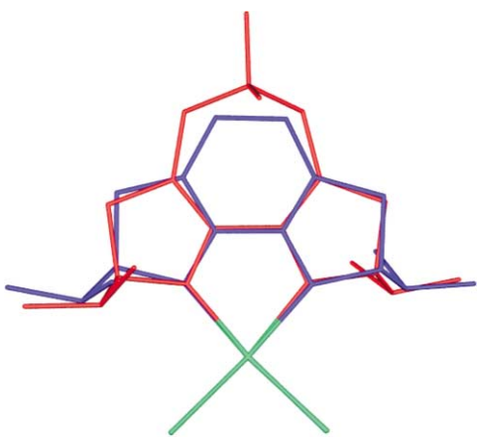


Fig. 5 Top view of a superimposition of the complexes **17** (blue) and **18** (red), obtained by superimposition of the Pd and two Cl atoms (green). Hydrogens are omitted for clarity.

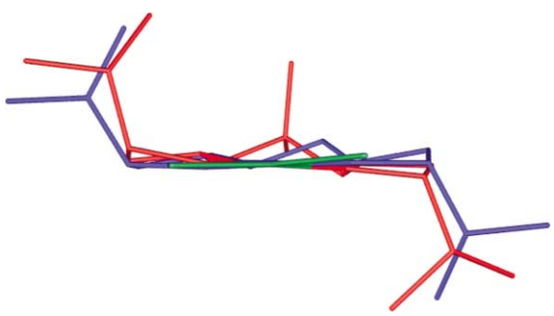
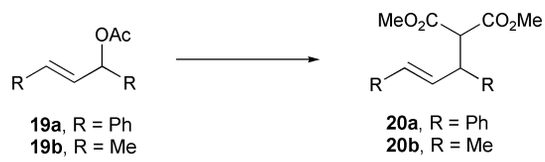


Fig. 6 View of a superimposition of the complexes **17** (blue) and **18** (red), obtained by superimposition of the Pd and two Cl atoms (green), along the Pd coordination plane. Hydrogens are omitted for clarity.

The very close similarity in bond angles for the complexes **18** and **19** (Table 2), containing quite dissimilar ligands, is striking. Evidently, our 5,7,5 tricyclic ligand happens to match almost perfectly the coordination geometry adopted by the relatively unconstrained bicyclic ligand in complex **19**.

Use of biimidazolines in Pd-catalysed allylations

Compared to oxazolines, there are very few reports of the use of imidazolines as ligands in metal-catalysed reactions.[6–9,15,16] To explore the potential of the new imidazolines as ligands, and to provide a comparison with the analogous oxazolines, we first tested them in a 'benchmark' reaction, the Pd-catalysed asymmetric allylation of malonate using the standard substrates **21a** and **21b** (Scheme 2).[25,26] A wide variety of N,N ligands have previously been used in this reaction.[27,28]



19a, R = Ph
19b, R = Me

20a, R = Ph
20b, R = Me

Scheme 2 Asymmetric allylation reactions.

Two conventional reaction protocols (use of bistrimethylsilyl-acetamide/KOAc, and use of preformed dimethyl sodiomalonate) were investigated. Poor yields were obtained using the BSA method. However, conversions were much better using preformed malonate ion (THF, 50 °C), and the results are shown in Table 3, along with the results reported for an analogous bioxazoline **1a** (R = Bn) under the same conditions. Other bioxazolines were reported to be ineffective under these conditions,[19a] and the one bioxazoline that was tested failed to give allylation product under the BSA conditions.[19b] In contrast, the allylation proceeded successfully with all the biimidazolines **12**–**14**, indicating that the biimidazolines are more effective ligands than the bioxazolines in this reaction. The biimidazoline ligands would be expected to bind more strongly to transition metals than bioxazolines because they are substantially more nucleophilic and because of the entropic advantage conferred by the conformational rigidity of the tricyclic structures. All the reactions were carried out for the same length of time (60 h), so the yields reported in Table 3 provide an indication of the relatives rates of the reactions rather than the optimum yields that might be achieved.

With biimidazoline ligands **12**, **13** and **14**, high conversions and moderate to good ee values were obtained with the diphenylallyl substrate **21a** (Table 3). As expected, the absolute configuration of the product was the same as obtained using the bioxazoline **1a**.[19a] The 5,7,5 tricyclic ligands **13** and **14** gave noticeably higher enantioselectivity than the 5,6,5 systems of **12**. The best enantioselectivity was achieved with the leucine derivative **14a**, which was slightly better than the only effective bioxazoline **1a**. We suggest that the improved selectivity with the 5,7,5 ligands is due, at least in part, to the decrease in the Pd–N bond lengths and the ψ angles in these systems (Fig. 5), which moves the R groups at the chiral centres slightly closer to the metal, with the result that they interact more effectively with the π-allyl and alkene ligands in the key reaction intermediates. The difference in the orientation of the isopropyl groups (Fig. 6) could also be a significant factor, if it persists in solution.

The two ligands **16a** and **16b** bearing additional stereocentres on the central ring were of interest because, although we did not expect the remote centres to influence the enantioselectivity directly, we wondered if the phenyl groups might have an indirect effect by reducing the conformational freedom of the

isobutyl groups. Although the phenyl groups were pseudoaxial (see above), no such effect was observed, and both ligands gave essentially identical enantioselectivity to the unsubstituted analogue **12a**. However, the result for **16a** has to be treated with caution because the ligand was slightly contaminated with an unknown impurity.

The pentenyl acetate **21b** reacted more slowly and gave lower enantioselectivity, though the reduction in ee values with the less bulky substrate is much smaller than found with many chiral ligands. The most notable trend was a clear decrease in yields in the series ethylene bridged **12** > propylene bridged **13** > dimethylpropylene bridged **14**, as the ligands became more strongly donating. The most basic ligands are expected to be similar to diamines in basicity and donor strength,[5] and although diamines have been used successfully in Pd-catalysed allylations,[27] they, like the biimidazolines, are sometimes ineffective with less reactive substrates like **21b**. It is clear that strong σ-donor ligands are not usually an appropriate choice for this substrate, presumably because they retard nucleophilic attack on the π-allyl intermediate.

Conclusions

These results confirm the potential of biimidazolines as ligands for asymmetric catalysis and provide important initial information on their donor properties. Certainly, much better chiral ligands are available for Pd-catalysed allylations, but the comparison between the biimidazolines and the analogous oxazolines is informative. The results indicate that the greater donor strength of the biimidazolines may be an advantage in some cases, as shown by the successful use of a wide variety of imidazolines in the Pd-catalysed allylation, in which most bioxazolines are ineffective. The results also illustrate the substantial variations in both reactivity and enantioselectivity, that may be achieved by tuning the N-1 substituents, an option that is not available with oxazolines. The variations in the yield of the allylation product **22b** is a clear demonstration of the strength of the effect of tuning the ligand donicity by altering the N-1 substituent.

The simple new synthetic route to enantiopure biimidazolines described above makes these compounds more readily accessible than before. Biimidazolines can now be added to the list of NN bidentate ligands that are readily available for use in catalytic asymmetric reactions, and further applications of these new ligands may be expected. A study of the related bisimidazolines **4**, analogues of bisoxazolines **2**, will be reported shortly.

Experimental

NMR spectra were recorded on Joel JNM-PMX-270, Varian Inova-300 and Varian Inova-5000 spectrometers. Tetramethylsilane was used as an internal reference (δ TMS = 0.0), and coupling constants are given in Hertz. IR spectra were recorded on a Mattson Galaxy 3000 Fourier Transform spectrometer. Melting points were recorded on a Gallenkamp electrothermal melting point apparatus and are uncorrected. Mass spectra were obtained using a Micromass Quattro micro instrument using electrospray ionisation. High resolution mass spectra were obtained using a VG Alto spectrometer. Elemental analysis was carried out in the Microanalytical Laboratories of the Chemistry Department, UCD. Optical rotations were determined using Perkin Elmer 241 and 343 polarimeters. Merck silica gel 60 F254 or Merck neutral aluminium oxide 60 F254 were used for thin layer chromatography. Column chromatography was carried out using Merck aluminium oxide 90 (Brockmann activity II to III) (1097) or Merck silica gel 60 (230–400 mesh) (9385). Solvents were dried and distilled according to literature procedures.

(*S*,*S*)-*N*,*N*′-Bis-(1-chloromethyl-3-methylbutyl)oxalamide, 9a. To a solution of (−)-(*S*)-2-amino-4-methylpentan-1-ol (L-leucinol; 4.46 g, 38.06 mmol) in toluene (150 cm^3) was added dimethyl oxalate (2.14 g, 18.13 mmol), and the mixture was heated at reflux for 5 h. After cooling to room temperature, hexane (150 cm^3) was added and the product was filtered off and washed with hexane. The hydroxy oxalamide **8a** was obtained as a white solid (4.49 g, 86%) which was used without further purification; mp 172–174 °C (from toluene); $[a]_D^{20}$ −27.7 (*c* 1.5, MeOH); found C, 58.0; H, 9.5; N, 9.6%; $C_{14}H_{24}N_4$ requires C, 58.3; H, 9.8; N, 9.7%; ν_{max} (KBr)/cm^{-1} 3285, 2953, 2873, 1655, 1531, 1250, 1215, 1060, 1031 and 780; δ_H (300 MHz; DMSO-d_6; Me_4Si) 0.90 (6 H, d, *J* 6.4, Me), 0.91 (6 H, d, *J* 6.4, Me), 1.29–1.54 (6 H, m, Me_2CHCH_2), 3.35–3.45 (4 H, m, CH_2O), 3.81–3.88 (2 H, m, CHN), 4.77 (2 H, t, *J* 5.6, OH) and 8.28 (2 H, d, *J* 9.4, NH); δ_C (75.4 MHz; DMSO-d_6; Me_4Si) 22.6 (CH_3), 23.9 (CH_3), 25.0 ($CH(CH_3)_2$), 40.2 ($CHCH_2CH$), 50.3 (NHCH), 64.0 (CH_2OH) and 160.2 (OCNH); *m*/*z* (ES+) 289.1 (M^+ + 1). The oxalamide **8a** (4.49 g, 15.57 mmol) was suspended in toluene (60 cm^3) and thionyl chloride (2.5 cm^3, 34.35 mmol) added. After heating at 90 °C for 4 h the solution was cooled to room temperature and poured onto cold 20% aqueous KOH (100 cm^3). The product was extracted with CH_2Cl_2 (3 × 100 cm^3), washed with saturated $NaHCO_3$ (100 cm^3), dried over $NaSO_4$, and concentrated under vacuum. The chlorooxalamide **9a** was obtained as a white solid (4.96 g, 98%) and could be used without further purification. mp 131–132 °C (from toluene/hexane); $[a]_D^{20}$ −68.8 (*c* 2, $CHCl_3$); ν_{max} (KBr)/cm^{-1} 3289, 2959, 2873, 1657, 1525, 1256, 1186, 775 and 729; δ_H (300 MHz; $CDCl_3$; Me_4Si) 0.97 (6 H, d, *J* 6.4, Me), 0.99 (6 H, d, *J* 6.2, Me), 1.54–1.62 (6 H, m, Me_2CHCH_2), 3.63 (2 H, dd, *J* 4.2 and 11.2), 3.72 (2 H, dd, *J* 4.2 and 11.2), 4.21–4.32 (2 H, m, CHN) and 5.56 (2 H, d *J* 9.0, NH); δ_C (75.4 MHz; $CDCl_3$; Me_4Si) 22.2 (Me), 22.9 (Me), 24.7 (Me_2C), 40.8 ($CHCH_2$), 47.6 (CH_2Cl), 48.7 (CHN) and 159.2 (C=O); *m*/*z* (ES+) 325.2 (M^+ + 1).

(*S*,*S*)-2,9-Diisopropyl-2,3,5,6,8,9-hexahydrodiimidazo[1,2-*a*;2′,1′-*c*]pyrazine, 12b. To a solution of *N*,*N*′-bis-(l-chloromethyl-2-methyl-propyl)oxalamide **9b**[19d] (400 mg, 1.35 mmol) in toluene (10 cm^3) was added PCl_5 (672 mg, 3.23 mmol) and the mixture was heated in an N_2 atmosphere for 4.5 h at 85 °C. The solvent was removed under vacuum to give the crude imidoyl chloride, as an oil; δ_H (300 MHz; $CDCl_3$; Me_4Si) 0.88 (6 H, d, *J* 6.9, CH_3), 0.90 (6 H, d, *J* 6.9, CH_3), 1.99–2.10 (2 H, m, $CH(CH_3)_2$), 3.57–3.71 (4 H, m, CH_2) and 3.94 (2 H, ddd, *J* 4.4, 5.6 and 7.9, NCH); δ_C (75.4 MHz; $CDCl_3$; Me_4Si) 18.1 (CH_3), 18.5 (CH_3), 31.5 ($CH(CH_3)_2$), 45.5 (CH_2Cl), 71.0 (NCH) and 139.0 (ClCN); *m*/*z* (EI) 334 (M^+). The imidoyl chloride was dissolved in CH_3CN (10 cm^3), Et_3N (0.56 cm^3, 4.04 mmol) was added, and the mixture was stirred for 5 min under N_2. A solution of Et_3N (0.56 cm^3, 4.04 mmol) and ethylenediamine (0.27 cm^3, 4.05 mmol) in dry CH_3CN (≈1 cm^3) was added and the mixture was heated to reflux in an atmosphere of N_2. After 3.5 h the solution was cooled to room temperature, and water (100 cm^3) and CH_2Cl_2 (40 cm^3) were added. The organic phase was separated and the aqueous phase extracted with CH_2Cl_2 (2 × 40 cm^3). The combined organic phases were dried over $MgSO_4$, filtered and concentrated under vacuum. The crude product was purified by column chromatography on alumina (EtOAc/petroleum ether, 80/20) to give the biimidazoline **12b**, as a white solid (230 mg, 70%); mp 120–122 °C (from EtOAc/hexane); $[a]_D^{20}$ +111.6 (*c* 2, $CHCl_3$); found C, 67.5; H, 9.6; N, 22.4%; $C_{14}H_{24}N_4$ requires C, 67.7; H, 9.75; N, 22.6%; ν_{max} (KBr)/cm^{-1} 2951, 2867, 2827, 1630, 1452, 1423, 1346, 1254 and 1171; δ_H (300 MHz; $CDCl_3$; Me_4Si) 0.91 (6 H, d, *J* 6.7, CH_3), 1.10 (6 H, d, *J* 6.7, CH_3), 1.78–1.87 (2 H, m, $CH(CH_3)_2$), 2.81 (2 H, dd, *J* 9.0 and 12.6, NCH_2), 3.17–3.30 (4 H, m, CH_2CH_2), 3.53 (2 H, apparent t, *J* 9.0, NCH_2) and 3.77 (2 H, ddd, *J* 7.6, 9.0, 12.6, NCH); δ_C (75.4 MHz; $CDCl_3$; Me_4Si) 18.8, 20.1, 33.0

($CH(CH_3)_2$), 45.4, 55.3, 72.3 (NCH) and 154.4 (NCN); *m*/*z* (EI) 248 (M^+).

(*S*,*S*)-2,9-Dibenzyl-2,3,5,6,8,9-hexahydrodiimidazo[1,2-*a*;2′,1′-*c*]pyrazine, 12c. Reaction of *N*,*N*′-Bis(l-benzyl-2-chloroethyl)oxalamide **9c**[19d] (700 mg, 1.78 mmol) with ethylenediamine (0.36 cm^3, 5.34 mmol), as for **12b**, gave the biimidazoline **12c** as a white solid (385 mg, 63%); mp 120–122 °C (from EtOAc/hexane); $[a]_D^{20}$ +54.9 (*c* 2, $CHCl_3$); found C, 76.5; H, 6.9; N, 16.15%; $C_{22}H_{24}N_4$ requires C, 76.7; H, 7.0; N, 16.3%; ν_{max} (KBr)/cm^{-1} 2921, 2359, 1612, 1437, 1355, 1253, 1155, 1056, 759 and 703; δ_H (300 MHz; $CDCl_3$; Me_4Si) 2.70 (2 H, dd, *J* 9.3, 13.8, CH_2Ph), 2.94 (2 H, apparent t, *J* 9.4, NCH_2), 3.10–3.20 (4 H, m, CH_2CH_2), 3.31–3.39 (4 H, m, CH_2Ph and NCH_2), 4.30–4.41 (2 H, ddd, *J* 5.1, 9.4, 14.5, NCH) and 7.09–7.23 (10 H, m, Ar–H); δ_C (75.4 MHz; $CDCl_3$; Me_4Si) 41.5 (CH_2Ph), 45.0 (NCH_2), 56.7 (NCH_2), 67.2 (NCH), 126.2, 128.4, 129.2, 138.8 and 154.5 (NCN); *m*/*z* (EI) 344 (M^+).

(*S*,*S*)-2,9-Diisobutyl-2,3,5,6,8,9-hexahydro-diimidazo[1,2-*a*;2′,1′-*c*]pyrazine, 12a. Reaction of *N*,*N*′-bis(l-chloromethyl-3-methylbutyl)oxalamide **9a** (500 mg, 1.54 mmol) with ethylenediamine (0.31 cm^3, 4.62 mmol), as for **12b**, and purification using column chromatography on alumina (EtOAc/petroleum ether, 80/20) gave the biimidazoline **12a** as a white solid (280 mg, 66%); mp 115–117 °C (from toluene/hexane); $[a]_D^{20}$ +49.2 (*c* 2, $CHCl_3$); found C, 69.2; H, 10.05; N, 20.2%; $C_{16}H_{28}N_4$ requires C, 69.5; H, 10.2; N, 20.3%; ν_{max} (KBr)/cm^{-1} 2961, 2866, 1626, 1487, 1433, 1348, 1283 and 1171; δ_H (300 MHz; $CDCl_3$; Me_4Si) 0.91 (6 H, d, *J* 6.6, CH_3), 0.93 (6 H, d, *J* 6.6, CH_3), 1.32 (2 H, apparent dt, *J* 7.2 and 13.6, $CH_2CH(CH_3)_2$), 1.75 (2 H, apparent dt, *J* 7.2, 13.6, $CH_2CH(CH_3)_2$), 1.87–1.97 (2 H, m, $CH(CH_3)_2$), 2.73 (2 H, dd, *J* 8.7 and 11.9, NCH_2), 3.14–3.27 (4 H, m, CH_2CH_2), 3.55 (2 H, apparent t, *J* 8.7, NCH_2) and 3.99–4.11 (2 H, m, NCH); δ_C (75.4 MHz; $CDCl_3$; Me_4Si) 22.6 (CH_3), 22.9 (CH_3), 25.3 $CH(CH_3)_2$, 45.3 (CH_2), 45.5 (CH_2), 58.3 (CH_2), 64.2 (NCH) and 154.3 (NCN); *m*/*z* (ES+) 277.2 ($M^+ + 1$).

(*S*,*S*)-2,8-Diisopropyl-2,3,5,6,7,8-hexahydro-4*H*-1,3a,6a,9-tetraazacyclopenta[*e*]azulene, 13b. Reaction of *N*,*N*′-bis(l-chloromethyl-2-methylpropyl)-oxalamide **9b**[19d] (700 mg, 2.36 mmol) with propane-1,3-diamine (0.6 cm^3, 7.08 mmol), as for **12b**, and purification using column chromatography on alumina (EtOAc/Et_3N/MeOH, 92/5/3) gave biimidazoline **13a** as a pale yellow oil that largely solidified on standing (185 mg, 30%); mp 118–119 °C (from hexane); $[a]_D^{20}$ −49.6 (*c* 0.56, $CHCl_3$); found C, 68.4; H, 9.95; N, 21.3%; $C_{15}H_{26}N_4$ requires C, 68.7; H, 10.0; N, 21.35%; ν_{max} (KBr)/cm^{-1} 2950, 2884, 1600, 1444, 1361, 1252 and 1175; δ_H (300 MHz; $CDCl_3$; Me_4Si) 0.88 (6 H, d, *J* 6.7, CH_3), 1.05 (6 H, d, *J* 6.7, CH_3), 1.80–1.88 (4 H, m, $CH(CH_3)_2$ and $CH_2CH_2CH_2$), 3.09 (2 H, dd, *J* 8.9 and 10.6, NCH_2), 3.19–3.25 (4 H, m, $CH_2CH_2CH_2$), 3.50 (2 H, dd, *J* 8.9, 10.1, NCH_2) and 3.78 (2 H, apparent dt, *J* 7.0, 10.3, NCH); δ_C (75.4 MHz; $CDCl_3$; Me_4Si) 18.7 (CH_3), 20.0 (CH_3), 26.8 (CH_2), 33.1 $CH(CH_3)_2$), 44.0 (CH_2), 56.0 (CH_2), 71.8 (NCH) and 158.2 (NCN) *m*/*z* (ES+) 263.1 ($M^+ + 1$).

(*S*,*S*)-2,8-Dibenzyl-2,3,5,6,7,8-hexahydro-4*H*-1,3a,6a,9-tetraazacyclopenta[*e*]azulene, 13c. Reaction of *N*,*N*′-bis(l-benzyl-2-chloroethyl)oxalamide **9c**[19d] (400 mg, 1.02 mmol) with propane-1,3-diamine (0.26 cm^3, 3.05 mmol), as for **12b**, and purification using column chromatography on alumina (EtOAc/Et_3N/MeOH, 85/5/10) gave the biimidazoline **13c** as a pale yellow oil (110 mg, 30%); $[a]_D^{20}$ +8.2 (*c* 1, $CHCl_3$), ν_{max} (KBr)/cm^{-1} 2925, 2853, 1677, 1627, 1454, 1030 and 751; δ_H (300 MHz; $CDCl_3$; Me_4Si) 1.76 (2 H, apparent quintet, *J* 6.4, $CH_2CH_2CH_2$), 2.68 (2 H, dd, *J* 9.5 and 13.7, $PhCH_2$), 3.00–3.17 (6 H, m, $CH_2CH_2CH_2$, NCH_2), 3.28 (2 H, dd, *J* 4.6 and 13.7, CH_2Ph), 3.40 (2 H, apparent t, *J* 9.5, NCH_2), 4.29–4.39 (2 H, apparent dq, *J* 4.6 and 9.5, NCH) and 7.17–7.30 (10 H, m, Ar–H); δ_C (75.4 MHz; $CDCl_3$; Me_4Si) 26.9, 41.8, 44.3, 57.9, 66.6 (NCH), 126.4, 128.6, 129.5, 139.2 and 158.4 (NCN); *m*/*z* (ES+) 359.2220 ($M^+ + 1$). $C_{23}H_{27}N_4$ requires 359.2236.

(*S*,*S*)-2,8-Diisobutyl-5,5-dimethyl-2,3,5,6,7,8-hexahydro-4*H*-1,3a,6a-tetraazacyclopenta[*e*]azulene, 14a. Reaction of *N*,*N*′-bis-(l-chloromethyl-3-methylbutyl)oxalamide **9a** (550 mg, 1.69 mmol) with 2,2-dimethylpropane-1,3-diamine (0.61 cm^3, 5.07mmol), as for **12b**, and ppurification using column chromatography on alumina (EtOAc/petroleum ether, 80/20) gave the biimidazoline **14a** as a clear oil that largely solidified on standing (215 mg, 40%); mp 57–59 °C; $[a]_D^{23}$ −42.3 (*c* 1.94, $CHCl_3$); ν_{max} (KBr)/cm^{-1} 2959, 2932, 2872, 1681, 1626, 1467, 1019, 757 and 666; δ_H (300 MHz; $CDCl_3$; Me_4Si) 0.90 (6 H, d, *J* 6.2, CH_3), 0.92 (6 H, d, *J* 6.2, CH_3), 0.95 (6 H, s, $C(CH_3)_2$), 1.29 (2 H, apparent dt, *J* 13.5 and 6.9, $CH_2CH(CH_3)_2$), 1.72–1.89 (4 H, m, $CH_2CH(CH_3)_2$), 2.62 (2 H, d, *J* 13.5, $CH_2C(CH_3)_2CH_2$), 2.91 (2 H, dd, *J* 8.8, 10.5, NCH_2), 3.02 (2 H, d, *J* 13.5, $CH_2C(CH_3)_2CH_2$), 3.64 (2 H, apparent t, *J* 8.8, NCH_2) and 3.99–4.11 (2 H, m, NCH); δ_C (75.4 MHz; $CDCl_3$; Me_4Si) 22.7 and 22.8 ($CH(CH_3)_2$), 24.7 ($CH(CH_3)_2$), 25.2 ($C(CH_3)_2$), 37.2 ($C(CH_3)_2$), 45.5 (CH_2), 56.2 (CH_2), 60.0 (CH_2), 63.8 (NCH) and 157.9 (NCN); *m*/*z* (ES+) 319.2860 ($M^+ + 1$). $C_{19}H_{35}N_4$ requires 319.2862.

Further characterisation was accomplished by forming a $ZnCl_2$ complex. The crude biimidazoline **14a**, prepared from *N*,*N*′-bis-(l-chloromethyl-3-methylbutyl)oxalamide (500 mg, 1.54 mmol), was dissolved in $CHCl_3$ (15 cm^3) and $ZnCl_2$ (210 mg, 1.54 mmol) was added. The mixture was stirred at RT under N_2, and the progress of the reaction was monitored by TLC and by the disappearance of $ZnCl_2$. After 1.5 h the solution was filtered through a small plug of silica which was flushed with EtOAc, and the solvent was removed under reduced pressure to give a yellow oil. The oil was purified using column chromatography on silica (EtOAc/petroleum spirits, 80/20) to give a white solid (200 mg, 29%) which was recrystallised from EtOAc; mp 182 °C (decomposition); found C, 49.9; H, 7.1; Cl, 15.5; N, 12.2; Zn, 14.5%; $C_{19}H_{34}Cl_2N_4Zn$ requires C, 50.2; H, 7.5; Cl, 15.6; N, 12.3; Zn, 14.4%; δ_H (300 MHz; $CDCl_3$; Me_4Si) 0.94 (6 H, d, *J* 6.3, CH_3), 0.97 (6 H, d, *J* 6.3, CH_3), 1.10 (6 H, s, $C(CH_3)_2$), 1.36–1.44 (2 H, m, $CH_2CH(CH_3)_2$), 1.82–1.91 (4 H, m, $CH_2CH(CH_3)_2$), 3.07 (2 H, d, *J* 13.7, $CH_2C(CH_3)_2CH_2$), 3.14 (2 H, d, *J* 13.7, $CH_2C(CH_3)_2CH_2$), 3.39 (2 H, apparent t, *J* 10.1, NCH_2), 3.91 (2 H, dd, *J* 10.1 and 11.1, NCH_2) and 4.22–4.33 (2 H, m, NCH).

(*S*,*S*)-2,8-Diisopropyl-5,5-dimethyl-2,3,5,6,7,8-hexahydro-4*H*-1,3a,6a-tetraaza-cyclopenta[*e*]azulene, 14b. Reaction of *N*,*N*′-bis-(l-chloromethyl-2-methylpropyl)oxalamide **9b**[19d] (700 mg, 2.36 mmol) with 2,2-dimethylpropane-1,3-diamine (0.85 cm^3, 7.07 mmol), as for **12b**, and purification using column chromatography on alumina (EtOAc/Et_3N, 95/5,) gave the biimidazoline **14b** as a clear oil that largely solidified on standing (305 mg, 45%); mp 87–88 °C (from pentane); $[a]_D^{20}$ −104.0 (*c* 0.8, $CHCl_3$); found C, 70.1; H, 10.35; N, 19.2%; $C_{17}H_{30}N_4$ requires C, 70.3; H, 10.4; N, 19.3%; ν_{max} (KBr)/cm^{-1} 2956, 2871, 1677, 1605, 1464, 1386, 1262 and 1127; δ_H (300 MHz; $CDCl_3$; Me_4Si) 0.87 (6 H, d, *J* 6.7, $CH(CH_3)_2$), 0.94 (6 H, s, $C(CH_3)_2$), 1.04 (6 H, d, *J* 6.7, $CH(CH_3)_2$), 1.80–1.87 (2 H, m, $CH(CH_3)_2$), 2.76 (2 H, d, *J* 13.8, $CH_2C(CH_3)_2CH_2$), 2.91 (2 H, d, *J* 13.8, $CH_2C(CH_3)_2CH_2$), 3.13 (2 H, dd, *J* 8.8, 10.2, NCH_2), 3.51 (2 H, dd, *J* 8.8, 10.2, NCH_2), 3.82 (2 H, apparent dt, *J* 6.7, 10.2, NCH); δ_C (75.4 MHz; $CDCl_3$; Me_4Si) 18.6 ($CH(CH_3)_2$), 19.8 ($CH(CH_3)_2$), 24.9 ($C(CH_3)_2$), 33.2 ($CH(CH_3)_2$), 37.6 ($C(CH_3)_2$), 56.3 (CH_2), 56.7 (CH_2), 71.9 (NCH) and 158.1 (NCN); *m*/*z* (ES+) 291.1 ($M^+ + 1$).

(*S*,*S*)-2,11-Diisopropyl-2,3,10,11-tetrahydrodiimidazo[1,2-*a*;2′,1′-*c*]quinoxaline, 15. A solution of *ortho*-phenylenediamine (0.6 g, 5.3 mmol) and triethylamine (2.7 cm^3, 19.2 mmol) in

acetonitrile (20 cm^3) was added dropwise at 0 °C to a solution of the bisimidoyl chloride, prepared as described for **12b**, (1.6 g, 4.8 mmol), in acetonitrile (30 cm^3). The reaction mixture was refluxed for 24 h and worked up as before. The crude product was twice chromatographed on alumina (EtOAc) to give the biimidazoline **15** (≈90% pure) (0.35 g, 25%); δ_H (300 MHz; $CDCl_3$; Me_4Si) 0.95 (6 H, d, *J* 6.9, CH_3), 1.06 (6 H, d, *J* 6.9, CH_3), 1.88–1.99 (2 H, m, C*H*$(CH_3)_2$), 3.60 (2 H, apparent t, *J* 9.8, NCH_2), 3.93 (2 H, dd, *J* 9.8, 11.1, NCH_2), 4.23 (2 H, ddd, *J* 6.1, 9.8, 11.1, NCH), 6.66 (2 H, m, 5-H, 8-H), 6.95 (2 H, m, 6-H, 7-H); δ_C (67.8 MHz; $CDCl_3$; Me_4Si)18.3 (CH_3), 19.0 (CH_3), 33.3 (*C*H$(CH_3)_2$), 48.8 (CH_2N), 72.0 (CHN), 111.4 (C-6, C-7), 121.2 (C-5, C-8), 127.2 (NCHPh) and 147.1 (NCN); *m*/*z* (EI) 295 ($M^+ - 1$).

2,9-Diisobutyl-5,6-diphenyl-2,3,5,6,8,9-hexahydrodiimidazo-[1,2-*a*;2′,1′-*c*]pyrazines, 16a and 16b. Reaction of *N*,*N*′-bis(l-chloromethyl-3-methylbutyl)oxalamide **9a** (400 mg, 1.23 mmol) with stilbenediamine (400 mg, 1.88 mmol), as for **12b**, and purification using column chromatography on alumina (EtOAc/petroleum ether, 20/80) gave the biimidazoline **16a** (R_f = 0.24) as a pale yellow solid (105 mg, 20%, slightly contaminated with an unknown impurity) and biimidazoline **16b** (R_f = 0.17) as a pale yellow solid (109 mg, 21%).

16a ν_{max} (KBr)/cm^{-1} 2954, 2937, 2867, 1641, 1465, 1412, 1275, 1192, 753 and 698; δ_H (300 MHz; $CDCl_3$; Me_4Si) 0.88 (6 H, d, *J* 6.4, CH_3), 0.89 (6 H, d, *J* 6.4, CH_3), 1.23–1.31 (2 H, m, C*H*$_2$CH$(CH_3)_2$), 1.74–1.89 (4 H, m, C*H*$_2$C*H*$(CH_3)_2$), 2.41 (2 H, dd, *J* 8.9 and 13.4, NCH_2), 3.31 (2 H, apparent t, *J* 8.9, NCH_2), 4.00–4.19 (2 H, m, NCH), 4.05 (2 H, s, CHPh), 6.94–6.97 (4 H, m, Ar–H) and 7.15–7.39 (6 H, m, Ar–H); δ_C (75.4 MHz; $CDCl_3$; Me_4Si) 22.7 (CH_3), 22.8 (CH_3), 25.3 (*C*H$(CH_3)_2$), 45.5 (CH_2), 57.7 (CH_2), 64.0 (CH), 68.9 (CH), 128.1, 128.3, 128.4, 137.0 and 154.2 (NCN);); *m*/*z* (ES+) 429.3032 ($M^+ + 1$). $C_{28}H_{37}N_4$ requires 429.3018.

16b mp 98–100 °C (from pentane); $[a]_D^{20}$ −151 (*c* 0.77, $CHCl_3$); ν_{max} (KBr)/cm^{-1} 2955, 2927, 2856, 1522, 1496, 1455, 1251, 751 and 703; δ_H (300 MHz; $CDCl_3$; Me_4Si) 0.90 (6 H, d, *J* 6.6, CH_3), 0.95 (6 H, d, *J* 6.6, CH_3), 1.23–1.31 (2 H, m, C*H*$_2$CH$(CH_3)_2$), 1.68 (2 H, apparent dt, *J* 13.9 and 6.6, C*H*$_2$CH$(CH_3)_2$), 1.84–1.93 (2 H, m, C*H*$(CH_3)_2$), 2.99 (2 H, dd, *J* 5.5 and 9.3, NCH_2), 3.08 (2 H, apparent t, *J* 9.3, NCH_2), 4.18–4.24 (2 H, m, NCH), 4.20 (2 H, s, CHPh), 7.02–7.04 (4 H, m, Ar–H) and 7.25–7.29 (6 H, m, Ar–H); δ_C (75.4 MHz; $CDCl_3$; Me_4Si) 22.5 (CH_3), 23.0 (CH_3), 25.0 (*C*H$(CH_3)_2$), 44.8 (CH_2), 55.6 (CH_2), 63.0 (CH), 67.5 (CH), 127.8, 128.3, 128.5, 137.7 and 153.5 (NCN); *m*/*z* (ES+) 429.3032 ($M^+ + 1$). $C_{28}H_{37}N_4$ requires 429.3018.

(*S*,*S*)-2,9-Diisopropyl-2,3,5,6,8,9-hexahydrodiimidazo[1,2-*a*;2′,1′-*c*]pyrazine $PdCl_2$ complex, 17. To a solution of the biimidazoline **12b** (40 mg, 1.61 mmol) in methanol (2 cm^3) was added a solution of $Pd_2Cl_2(PhCN)_2$ (62 mg, 1.61 mmol) in methanol (3 cm^3). A pale precipitate was observed. After 4 h stirring at RT, the precipitate was filtered off and washed with $CHCl_3$. mp 310 °C (decomposition) (from CH_3CN); δ_H (300 MHz; CD_3CN; Me_4Si) 0.93 (6 H, d, *J* 7.2, CH(C*H*$_3)_2$), 0.98 (6 H, d, *J* 6.9, CH(C*H*$_3)_2$), 2.54–2.62 (2 H, m, C*H*$(CH_3)_2$), 3.42–3.51 (2 H, m, CH_2CH_2), 3.59–3.68 (4 H, m, NCH_2), 4.16–4.22 (2 H, m, NCH).

(*S*,*S*)-2,8-Diisopropyl-5,5-dimethyl-2,3,5,6,7,8-hexahydro-4*H*-1,3a,6a-tetraazacyclopenta[*e*]azulene $PdCl_2$ complex, 18. To a solution of the biimidazoline **14b** (40 mg, 1.38 mmol) in methanol (2 cm^3) was added a solution of $Pd_2Cl_2(PhCN)_2$ (53 mg, 1.38 mmol) in methanol (3 cm^3). A pale precipitate was observed. After 4 h stirring at RT, the mixture was filtered through a small plug of cotton wool and the solvent removed under vacuum. The product was dissolved in $CHCl_3$ and the solution was filtered through Celite® and evaporated to give an orange solid; mp 210 °C (decomposition) (from CH_2Cl_2); δ_H (300 MHz; $CDCl_3$; Me_4Si) 0.82 (6 H, d, *J* 6.7, CH(C*H*$_3)_2$), 0.84 (6 H, d, *J* 7.0, CH(C*H*$_3)_2$), 1.07 (6 H, s, C$(CH_3)_2$), 2.85–2.89 (2 H, m, C*H*$(CH_3)_2$), 3.04 (2 H, d, *J* 13.7, C*H*$_2$C$(CH_3)_2$C*H*$_2$), 3.11 (2 H, d, *J* 13.7, C*H*$_2$C$(CH_3)_2$C*H*$_2$), 3.47 (2 H, dd, *J* 6.0 and 10.5, NCH_2), 3.75 (2 H, dd, *J* 10.5, 11.7, NCH_2), 4.17–4.23 (2 H, m, NCH).

Crystal structure determination of complex 17. Yellow plates were obtained by slow evaporation of a solution in acetonitrile.

Crystal data. $C_{14}H_{24}N_4Cl_2Pd$, *M* = 425.67, monoclinic, *a* = 6.1922(11), *b* = 13.083(2), *c* = 23.842(4) Å, *α* = 90, *β* = 93.628(3), *γ* = 90°, *U* = 1927.7(6) $Å^3$, *T* = 293(2) K, space group $P2_1$ (no. 4), *Z* = 4, *μ*(Mo-Kα) = 1.239 mm^{-1}, 30487 reflections measured, 8850 unique (R_{int} = 0.0446) which were used in all calculations, absolute structure parameter = 0.02(5), largest diff. peak and hole = 3.897 and −2.016 e $Å^{-3}$ (the 4 highest peaks are located within 1 Å of the Pd atom). The final $wR(F^2)$ was 0.1752 (all data).

Crystal structure determination of complex 18. Yellow plates were obtained by slow evaporation of a solution in dichloromethane.

Crystal data. $C_{18}H_{32}N_4Cl_4Pd$, *M* = 552.68, monoclinic, *a* = 6.8256(6), *b* = 13.1722(11), *c* = 13.0599(11) Å, *α* = 90, *β* = 92.8580(10), *γ* = 90°, *U* = 1172.73(17) $Å^3$, *T* = 100(2) K, space group $P2_1$ (no. 4), *Z* = 2, *μ*(Mo-Kα) = 1.258 mm^{-1}, 10076 reflections measured, 5269 unique (R_{int} = 0.0216) which were used in all calculations, absolute structure parameter = −0.02(2). The final $wR(F^2)$ was 0.0682 (all data).

General procedure for asymmetric allylation using 3-acetoxy-1,3-diphenylprop-1-ene, 21a. The chiral ligand (9.9 μmol) and $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ (1.45 mg, 3.96 μmol) were dissolved in degassed THF (1 cm^3) under nitrogen and the solution was stirred at 40 °C to give a pale yellow solution. After 30 min a solution of the acetate **21a** (100 mg, 0.396 mmol) in THF (1 cm^3), sodium dimethylmalonate (67.2 mg, 0.436 mmol), naphthalene (12.7 mg, 0.099 mmol) and THF (2 cm^3) were successively added and the mixture was degassed again. After 60 h the reaction was quenched with glacial acetic acid (0.3 cm^3), Et_2O (5 cm^3) was added and the mixture was washed with 20% $NaHCO_3$ (2 × 5 cm^3), water, and saturated brine, dried with $MgSO_4$, and concentrated *in vacuo* to give a yellow oil. Chemical conversion (%) was determined at this point by ^1H NMR using naphthalene as the internal standard. Purification by passage through a short column of silica gel afforded the malonate **22a** as a colourless oil, which crystallised on standing. Enantiomeric excess was determined by HPLC analysis: Chiralcel OD H, hexane/Pr^{i}OH (97.5/2.5), 0.5 cm^3 min^{-1}, 254 nm; $R_t(R)$ = 15.7 min, $R_t(S)$ = 16.8 min. The absolute configuration was determined by polarimetry.[19b]

General procedure for allylic alkylation using 4-acetoxypent-2-ene, 21b. The acetate **21b** (50.7 mg, 0.396 mmol) was used, following the procedure described for **21a**. The yield was determined by ^1H NMR using naphthalene as the internal standard. The crude product was then purified by flash chromatography on silica gel with petroleum spirits : diethyl ether 19 : 1 to give the malonate **22b** as a colourless oil. δ_H (300 MHz; $CDCl_3$; Me_4Si) 1.04 (3H, d, *J* 6.8 Hz, Me), 1.62 (3H, d, *J* 6.4 and 1.5, Me), 2.83–2.96 (1H, m, CH=CHC*H*Me), 3.25 (1H, d, *J* 9.1, C*H*$(CO_2Me)_2$), 3.68 (3H, s, OMe), 3.72 (3H, s, OMe), 5.33 (1H, ddd, *J* 15.2, 8.2 and 1.5, MeCH=C*H*) and 5.51 (1H, ddq, *J* 15.2, 0.7 and 6.4, MeC*H*=CH). The enantiomeric excess was determined by ^1H NMR spectroscopy by successive additions of 10 μL portions of a 0.1 M solution of $Eu(hfc)_3$ in $CDCl_3$ to a sample of **22b** (10 mg) until sufficient splitting of the doublet of doublets at 1.62 ppm was observed to determine the ratio by integration ($\Delta\delta \approx 0.1$ ppm). The absolute configuration was determined by polarimetry.[29]

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