Pergamon

Tetrahedron: *Asymmetry* 10 (1999) 4803–4810

TETRAHEDRON: *ASYMMETRY*

Design and synthesis of enantiopure 1-[1(*S*)-(2-pyridyl)alkyl]-2(*R*)-isopropylaziridines, new ligands for asymmetric catalysis

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Received 10 November 1999; accepted 8 December 1999

Abstract

Enantiopure 1-(2-pyridyl)alkyl aziridines were designed as bidentate ligands for asymmetric catalysis. Their synthesis involved the addition of organometallic reagents to the imine prepared from 2-pyridinealdehyde and an enantiopure β-aminoalcohol, followed by cyclisation of the β-aminoalcohol moiety to the aziridine ring. Two such ligands (N–N)* were prepared from (*S*)-valinol and converted to the complexes (η^3-allyl)(N–N)*$Pd^+SbF_6^-$, one of which was characterised by X-ray crystallography. Modest enantioselectivities were achieved in a representative Pd-catalysed allylic substitution reaction.

1. Introduction

Enantiopure bidentate nitrogen donors have found extensive use as ligands to transition metals in a number of asymmetric reactions,[1] for example, the palladium-catalysed allylic substitution and the copper-catalysed cyclopropanation of alkenes. The former reaction has been successfully performed using tertiary and secondary 1,2-diamines having C_1 or C_2 symmetry, including acyclic diamines,[2] sparteine,[3] (−)-α-isosparteine,[4] phenanthrolines,[5] 8-aminoquinoline derivatives,[6] and compounds containing two aza-heterocycles connected by a link or a tether: bis-pyridines,[5b,7] bis-aziridines,[8] bis-pyrrolidines,[9] bis-oxazolines,[10] 5-aza-semicorrins,[11] pyridine–oxazolines,[12] and pyridine–pyrrolidines.[5b,13] In particular, in the reaction of 1,3-diphenyl-2-propenyl acetate **1** with dimethyl malonate high enantiomeric excess (e.e.) was achieved for the product **2** using bis-aziridine or pyridine-containing molecules as ligands (N–N)* (Scheme 1).[8]

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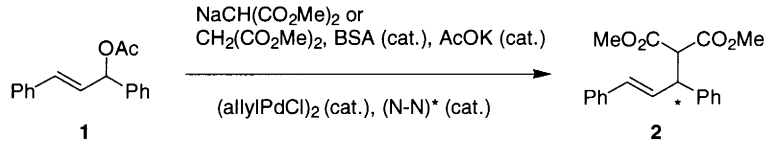
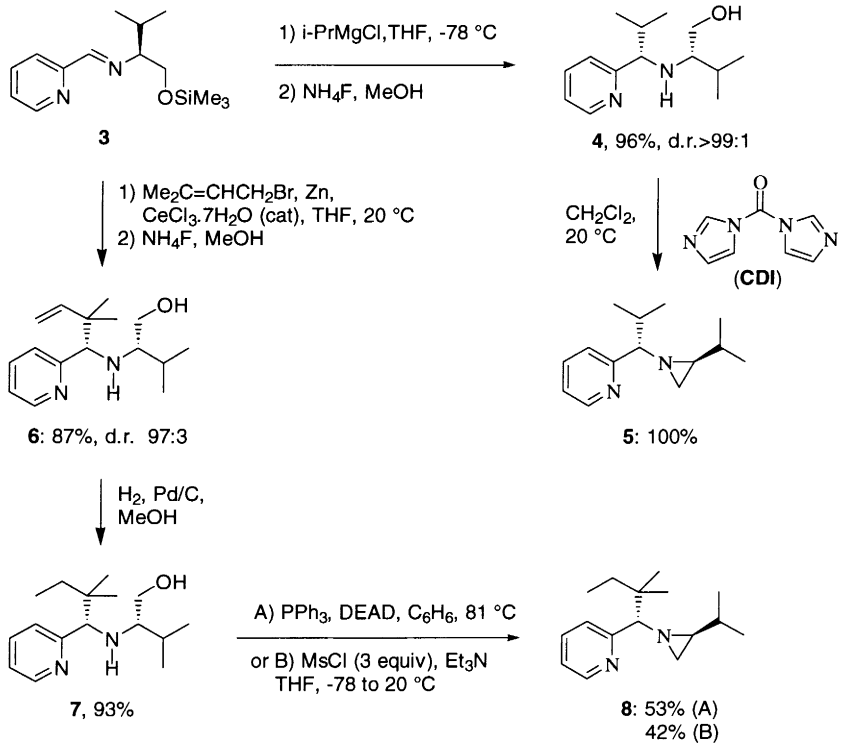
0957-4166/99/$ - see front matter
PII: S0957-4166(99)00571-6



Scheme 1.

2. Results and discussion

By considering the structural features of the above ligands, we envisaged that bidentate ligands containing the pyridine and aziridine rings should also be useful for the same synthetic purposes, and planned a simple two-step route for their preparation, based on our recently reported diastereoselective addition of organometallic reagents to (*S*)-*N*-(2-pyridylmethylene)-*O*-trimethylsilylvalinol[14] (Scheme 2). Accordingly, we added *iso*-propylmagnesium chloride to the imine **3** in THF solution at −78°C and isolated after acidic workup the known β-aminoalcohol **4**[14] with high yield and almost complete diastereoselectivity.



Scheme 2.

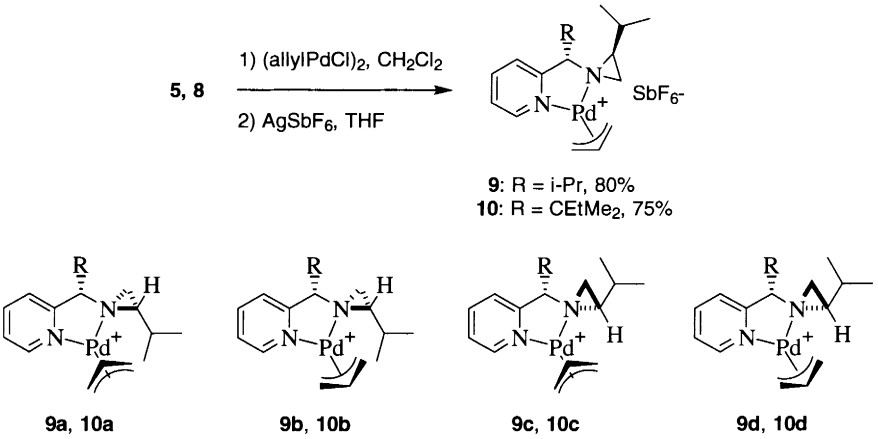
We found that the aziridine **5** was quickly and quantitatively formed from **4** by treatment with 1,1′-carbonyldiimidazole (**CDI**) in CH_2Cl_2 at room temperature. By simple filtration and aqueous workup to eliminate the imidazole produced, the aziridine **5** was obtained as a pure compound, avoiding purification by chromatography or distillation.

In order to introduce a more bulky substituent at the C-stereocentre and considering that the addition of *tert*-butyl organometallic reagents to the imine **3** was unsatisfactory,[14] we carried out the addition of 3-methyl-2-butenylzinc bromide to **3** at −78°C in THF and obtained, after desilylation with NH_4F in MeOH, the branched alkylation product **6** with high yield and high stereocontrol (d.r. >98:2). Moreover,

we successfully prepared **6** by the Barbier-type protocol we previously described for the allylation of analogous imines,[15] i.e. the in situ reaction of the imine with the allylic bromide, zinc powder and a catalytic amount of cerium trichloride heptahydrate in THF at 0–20°C. Following double bond hydrogenation, the saturated compound **7** was finally obtained.

Unfortunately, the desired aziridine **8** could not be obtained from **7** by reaction with **CDI**.[16] However, the classical Mitsunobu reaction allowed to prepare **8** with moderate yield, presumably owing to the partial loss of product during the chromatographic separation from the phosphinoxide formed as a by-product. A more convenient preparation of the aziridine **8** was achieved by reaction of **7** with 3 equiv. mesyl chloride in the presence of triethylamine at −78 to 20°C.[17]

The pyridine–aziridines **5** and **8** are prototypes of new ligands (N–N)* which are potentially useful for asymmetric catalysis, for example in the enantioselective palladium-catalysed allylic substitution reactions. These reactions are generally carried out using (N–N)* ligands and allylpalladium chloride dimer as precatalyst, but the preformed salt (allyl)(N–N*)Pd^+X^-, where X is a non-coordinating anion (BF_4^-, PF_6^-, ClO_4^-), can be used. A number of these salts have been prepared by several authors and examined by X-ray crystallographic and/or ^1H and ^{13}C NMR spectroscopic analyses, which gave information on the origin of the enantiocontrol. Hence, we prepared the cationic palladium complexes **9** and **10** as stable crystalline compounds by sequential treatment of the aziridines **5** and **8** with $(allylPdCl)_2$ and antimonium hexafluorophosphate, followed by crystallisation from methanol (Scheme 3).



Scheme 3.

The crystals of **9** were studied by X-ray diffraction and the structure of the cation is reported in Fig. 1. The π-allyl rotamers **9a** and **9b** were present in 75:25 ratio in the crystal. It is noteworthy that all the cations in the crystal have the *R* configuration of the aziridine nitrogen (N_2), as depicted in **9a** and **9b**; probably, the structures **9c** and **9d**, coming from the complexation of the aziridine (*S*)-nitrogen, suffer from the non-bonding interactions of the two isopropyl substituents. We presume that the same structures **9a** and **9b** are present in the solution, although with a different ratio (55:45) as determined in the $CDCl_3$ solution by ^1H and ^{13}C NMR spectroscopy. In the crystal, the allylic CH_2 termini occupied the same positions in **9a** and **9b** and the bond lengths with palladium were only slightly different: particularly, the C3 carbon *anti* to the aziridine nitrogen N2 formed a longer bond with Pd, compared to the C1 carbon *anti* to the pyridine nitrogen N1. The length of a Pd–C bond should be related to its weakness and, consequently, its reactivity.[18] Accordingly, the C1 and C3 carbons gave distinct ^{13}C absorptions, $\Delta\delta$ 0.2 ppm being observed in the salt **9**.

The lengths of the Pd–C and Pd–N bonds in the salt **9** (see Fig. 1) should be compared to those measur-

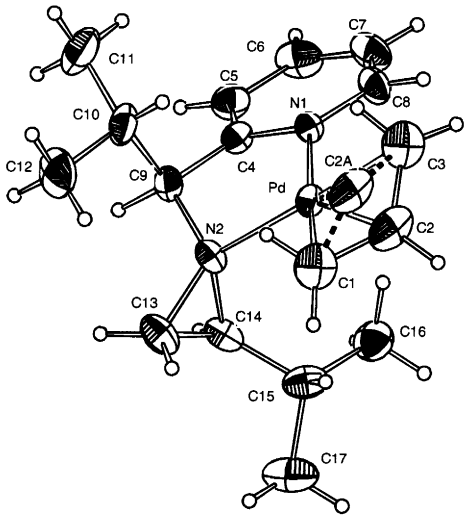


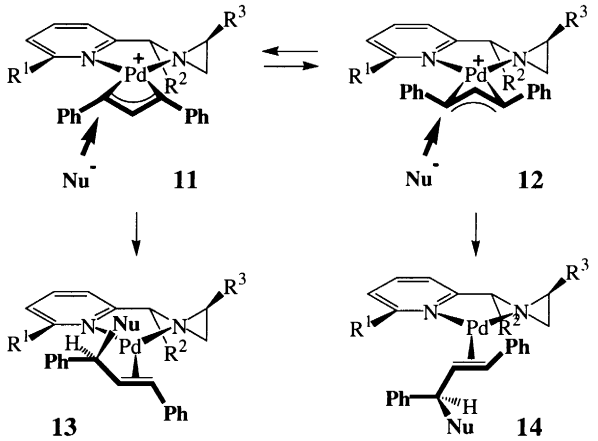
Fig. 1. X-Ray structure of the cation of **9a** and **9b**. The allyl ligand is disordered over two orientations (75% for **a** and 25% for **b**) with the outer carbons almost coincidental and the central one exhibiting a double image. Selected bond distances in **9a**: Pd–N_1 2.121(7) Å, Pd–N_2 2.110(6) Å, Pd–C_1 2.116(12) Å, Pd–C_3 2.138(12) Å, Pd–C_2 2.081(12) Å, C–C (allyl) 1.35, 1.37(2) Å

ed in the analogous complex [1-(2-pyridylmethyl)-2(*R*),5(*R*)-dimethylpyrrolidine](allyl)$Pd^+ClO_4^-$.[13a] In this salt the Pd–C(allyl) bonds have similar length (2.12 and 2.13 Å), but the Pd–N(pyridine, 2.08 Å) bond was shorter than the Pd–N(pyrrolidine, 2.15 Å) bond, contrary to the complex **9**, where Pd–N1 was longer than the Pd–N2.

The outcomes of preliminary reactions leading to compound **2** (Scheme 1) were not satisfactory. Enantiomeric excesses (e.e.) of 6 and 11% were obtained in the reactions performed using allylpalladium chloride dimer (2 mol%) and the aziridines **5** and **8** (6 mol%), respectively, in the presence of BSA and potassium acetate in CH_2Cl_2 at room temperature (32 h). However, by using the preformed sodium salt of diethyl malonate and the palladium salts **9** or **10** as the catalyst (2 mol%) in THF the e.e.s rose to 42 and 21%, respectively. In every case (*R*)-(+)-**2** was preferentially formed.

The observed sense of asymmetric induction can be explained as for the reactions catalysed by a pyrrolidine–pyridine ligand,[13] where the nucleophile was assumed to attack the most electrophilic allylic carbon (*anti* to pyrrolidine) of the most abundant isomeric complex. Apparently, our ligands **5** and **8** exert limited steric influence on the π-1,3-diphenylallyl ligand. Consequently, the low stereocontrol can be explained by the presence in solution of allylic rotamers having comparable reactivity, and/or by lack of regioselectivity in the nucleophilic attack.

However, we are confident that improved enantioselectivity will be achieved by proper modifications of the pyridine–aziridine ligand, as described in Scheme 4. While maintaining a bulky substituent R^2 at the stereocentre α to pyridine, which dictates the configuration of the aziridine nitrogen in the complexation step, the substituent R^3 can be varied: for example, starting from (*S*)-phenylglycinol, the steric and electronic features of the phenyl group can be exploited. Moreover, a new substituent R^1 introduced at C6 of the pyridine ring is expected to give a severe steric interaction with the allylic substituent (Ph). By these modifications, either the ratio of rotamers **11**/**12** will be increased and/or the allylic carbons will display a more differentiated electronic character, inducing the nucleophile to preferentially attack the allylic carbon *anti* to the aziridine nitrogen of the complex **11**.



Scheme 4.

3. Experimental

General methods, instrumentation and the preparations of the imine **3** and β-amino alcohol **4** were previously described.[14]

3.1. N-*[1-(*R*)-(2-Pyridyl)-2,2-dimethyl-3-butenyl]-(*S*)-valinol **6**

3,3-Dimethyl-2-propenyl bromide (0.67 g, 4.5 mmol) dissolved in dry THF (5 ml) was slowly added to the stirred suspension of zinc powder (0.39 g, 6 mmol), the imine **3** (0.79 g, 3 mmol) and $CeCl_3$–$7H_2O$ (0.112 g, 0.3 mmol) in dry THF (10 ml) under N_2.[15] After 3 h, the reaction mixture was quenched with NH_4Cl:NH_3 (1:1) solution (10 ml) and the organic phase was extracted with Et_2O. After usual workup, the organic product was treated with NH_4F (0.74 g, 20 mmol) in MeOH (10 ml) during 3 h. Most of MeOH was evaporated at reduced pressure, H_2O (10 ml) and NaOH pellets were added to reach pH 11, and the organic material was extracted with Et_2O (3×10 ml). The ethereal phase was dried over Na_2SO_4, then concentrated to leave the β-aminoalcohol **6** as an oil: 95%, d.r. 97:3 by GC–MS analysis; $[\alpha]_D^{20}$ −24.3 (*c* 1.2, $CHCl_3$). MS, *m/z* (relative intensity %) 193 (100, $M^+-C_5H_9$), 107 (80), 69 (13, C_5H_9), 231 (M^+-CH_2OH); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.6 (m, 1H, Py), 7.6 (m, 1H, Py), 7.15 (m, 2H, Py), 5.95 (dd, J_{cis}=10.8 Hz, J_{trans}=17.4 Hz, 1H, CH_2=C*H*), 5.35 (d, J_{cis}=10.7 Hz, 1H, CH_2=CH), 5.0 (d, J_{trans}=17.4 Hz, 1H, CH_2=CH), 3.9 and 3.4 (dd, *J*=3.9 and 10.9 Hz, 2H, CH_2OH), 3.45 (s, 1H, PyC*H*), 2.0 (m, 1H, NC*H*CH_2), 1.68 (m, 1H, C*H*Me_2), 1.05 and 1.0 (2 s, 6H, CMe_2), 0.78 and 0.72 (2 d, *J*=6.8 Hz, 6H, CH*Me*$_2$) ppm; ^{13}C NMR (300 MHz, $CDCl_3$, 20°C) δ 149.8, 136.2, 125.4, 123.0, 78.3, 70.4, 60.6, 42.7, 30.3, 26.1, 24.3, 20.8, 19.7 ppm.

3.2. N-*[1-(*R*)-(2-Pyridyl)-2,2-dimethyl-3-butyl]-(*S*)-valinol **7**

In a Parr apparatus, a mixture of compound **6** (0.680 g, 2.6 mmol), 10% $Pd(OH)_2$/C (0.078 g) and MeOH (36 ml) was submitted to a pressure of 50 psi H_2 overnight, then filtered over Celite. The solvent was evaporated at reduced pressure to leave the compound **7** as an oil: 0.640 g, 93%; $[\alpha]_D^{20}$ −15.5 (*c* 0.94, $CHCl_3$). MS, *m/z* (relative intensity %) 193 (100, $M^+-C_5H_{11}$), 107 (44), 162 (38, PyC_6H_{13}), 233 (M^+-CH_2OH); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.57 (d, *J*=4.8 Hz, 1H, Py), 7.57 (m, 1H, Py), 7.12 (m, 2H, Py), 3.59 (dd, *J*=3.6 and 10.5 Hz, 1H, CH_2OH), 3.40 (dd, *J*=3.6 and 10.0 Hz, 1H, CH_2OH), 3.39 (s, 1H, PyC*H*), 1.98 (m, 1H, NC*H*CH_2), 1.65 (broad, 2H, OH and NH), 1.58 (m, 1H, C*H*Me_2), 1.35 (m,

2H, C*H*$_2$CH$_3$), 0.93 and 0.83 (2 s, 6H, CMe$_2$), 0.85 (t, 3H, CH$_2$C*H*$_3$), 0.80 and 0.72 (2 d, *J*=6.9 Hz, 6H, CH*Me*$_2$) ppm. $C_{16}H_{28}N_2O$ required: C, 72.68; H, 10.16; N, 10.59%. Found: C, 72.65; H, 10.70; N, 10.56%.

3.3. 1-[1(S)-(2-Pyridyl)-2-methylpropyl]-2(R)-isopropylaziridine **5**

1,1′-Carbonyldiimidazole (**CDI**, 0.343 g, 2.11 mmol) was added to the solution of β-amino alcohol **4** (0.500 g, 2.11 mmol) in anhydrous CH_2Cl_2 (10 ml). The mixture was magnetically stirred at room temperature for 2 h, then quenched with H_2O (5 ml). The organic phase was separated, the aqueous layer was extracted with CH_2Cl_2 (5 ml), and the collected organic layers were dried over Na_2SO_4 and concentrated to leave the aziridine **5** as an oil: 0.457 g, 100%; $[\alpha]_D^{20}$ −18.9 (*c* 0.95, $CHCl_3$). MS, *m/z* (relative intensity) 175 (100, M^+-i-Pr), 92 (71), 119 (65), 84 (60), 146 (50), 120 (41), 135 (38), 118 (37), 107 (36), 56 (26); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.51 (m, 1H, Py), 7.66 (m, 1H, Py), 7.45 (m, 1H, Py), 7.15 (m, 1H, Py), 2.26 (m, 1H, NC*H*CH$_2$), 2.18 (d, *J*=8.5 Hz, 1H, PyCH), 1.76 (d, *J*=2.4 Hz, 1H, CHC*H*$_2$), 1.52 (d, *J*=6.0 Hz, 1H, CHC*H*$_2$), 1.12 (d, *J*=6.3 Hz, 3H, CH*Me*$_2$), 1.2–1.0 (m, 2H, C*H*Me$_2$), 0.74, 0.69 and 0.41 (3 d, *J*=6.6 Hz, 9H, CH*Me*$_2$) ppm. $C_{14}H_{22}N_2$ required: C, 77.01; H, 10.16; N, 12.83%. Found: C, 69.99; H, 10.18; N, 12.82%.

3.4. 1-[1(S)-(2-Pyridyl)-2,2-dimethylbutyl]-2(R)-isopropylaziridine **8**

Methanesulfonyl chloride (0.340 g, 3 mmol) dissolved in dry CH_2Cl_2 (1 ml) was slowly added to the magnetically stirred solution of the β-aminoalcohol **7** (0.264 g, 1 mmol) and triethylamine (0.505 g, 5 mmol) in CH_2Cl_2 (10 ml) at −78°C. The mixture was allowed to reach room temperature and stirred for a further 5 h, then aq. $NaHCO_3$ was added, the organic base was extracted with CH_2Cl_2 (3×10 ml). The collected organic phases were dried over Na_2SO_4 and concentrated to leave a residue which consisted of two non-miscible oils. The lighter clear oil was separated from the heavy dark oil by washing with Et_2O (2×5 ml). The solvent was evaporated to leave the pure aziridine **8** as a clear oil: 0.131 g, 53%; $[\alpha]_D^{25}$ −28.7 (*c* 0.6, $CHCl_3$). MS, *m/z* (relative intensity) 175 (100, $M^+-C_5H_{11}$), 146 (54), 92 (44), 119 (43), 107 (40); ^{1}H NMR (200 MHz, $CDCl_3$) δ 8.48 (m, 1H, Py), 7.70–7.50 (m, 2H, Py), 7.15 (m, 1H, Py), 2.52 (s, 1H, PyC*H*), 1.78 (d, *J*=3.6 Hz, 1H, CHC*H*$_2$), 1.50 (d, *J*=6.4 Hz, 1H, CHC*H*$_2$), 1.46–1.20 (m, 4H, NC*H*CH$_2$, C*H*$_2$Me, C*H*Me$_2$), 1.01 and 0.92 (2s, 6H, CEt*Me*$_2$), 0.85 (t, 3H, CH$_2$*Me*), 0.74 and 0.62 (2 d, *J*=6.8 and 6.7 Hz, CH*Me*$_2$) ppm. $C_{16}H_{26}N_2$ required: C, 77.99; H, 10.64; N, 11.37%. Found: C, 78.00; H, 10.65; N, 11.35%.

3.5. Preparation of the palladium complexes **9** and **10**. General procedure

To the solution of the aziridine **5** (0.160 g, 0.73 mmol) in anhydrous CH_2Cl_2 (15 ml) under an Ar atmosphere was added allylpalladium chloride dimer (0.128 g, 0.35 mmol) and the mixture was magnetically stirred for 1 h at 20°C, then a solution of $AgSbF_6$ (0.262 g, 0.76 mmol) in anhydrous THF (15 ml) was added, producing a white precipitate of AgCl. After 10 min the mixture was filtered over Celite and the filtered solution was washed with brine (10 ml), dried over Na_2SO_4, and concentrated to leave the crystals of complex **9**, which were purified by washing with cold MeOH (2 ml): 0.350 g, 80%. The complex was recrystallised slowly from MeOH at rt: $[\alpha]_D^{20}$ +6.0 (*c* 0.23, $CHCl_3$). The ^{1}H and ^{13}C NMR spectra showed the presence of two rotamers **a** and **b** of the π-allyl ligand in almost 1:1 ratio, so it was difficult to assign the adsorption to each rotamer; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.68 and 8.62 (2m, 1H, Py), 7.99 and 7.96 (2m, 1H, Py), 7.49 and 7.47 (2m, 1H, Py), 7.45 (m, 1H, Py), 5.84–5.64 (m, 1H,

CH allyl), 4.25 and 4.17 (2d, *J*=6.6 and 6.9 Hz, 1H, CH_2 allyl), 3.90 and 3.75 (2d, *J*=6.6 and 6.3 Hz, 1H, CH_2 allyl), 3.33 and 3.14 (2d, *J*=12.9 and 12.3 Hz, 1H, PyC*H*N), 3.26 and 3.17 (2d, *J*=6.3 and 7.2 Hz, 1H, CH_2 allyl), 3.28 and 2.84 (2d, *J*=12.6 and 14.4 Hz, 1H, CH_2 allyl), 2.54 (m, 1H, NC*H*CH_2), 2.63 and 2.32 (2m, 2H, NCHC*H*$_2$), 2.54 and 2.29 (2m, 1H, NCHC*H*$_2$), 1.95–1.77 (m, 1H, C*H*Me_2), 1.40 and 1.15 (2m, 1H, C*H*Me_2), 1.18, 1.10, 1.06, 1.01, 0.94, 0.92, 0.84 and 0.72 (8d, *J*=6.6 Hz, CH*Me*$_2$) ppm; ^{13}C NMR (200 MHz, $CDCl_3$) δ 160.7 and 160.5, 153.0 and 152.8, 139.6 and 139.5, 125.2 and 124.8, 117.6 and 117.5, 82.48, 61.6 and 61.5, 59.7 and 59.5, 51.3 and 51.1, 40.0 and 38.9, 34.8 and 34.4, 21.3 and 20.8, 20.0, 19.3 and 19.1, 18.7 and 18.5 ppm. $C_{17}H_{27}F_6N_2PdSb$ requires: C, 33.94; H, 4.52; N, 4.66%. Found: C, 33.96; H, 4.53; N, 4.65%.

The complex **10** was prepared in the same way from the aziridine **8**: 71%; $[\alpha]_D^{20}$ +9.6 (*c* 0.55, $CHCl_3$). The ^{1}H and ^{13}C NMR spectra showed the presence of two rotamers **a** and **b** of the π-allyl ligand in about a 1:1 ratio; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.68 and 8.61 (2m, 1H, Py), 7.98 (m, 1H, Py), 7.62 (m, 1H, Py), 7.46 (m, 1H, Py), 5.71 (m, 1H, CH allyl), 4.24 and 4.14 (2d, *J*=6.9 and 7.5 Hz, 1H, CH_2 allyl), 3.89 and 3.71 (2d, *J*=6.9 and 7.3 Hz, 1H, CH_2 allyl), 3.38 and 3.33 (2s, 1H, PyC*H*N), 3.26 and 3.07 (2m, 2H, CH_2 allyl), 2.80 (m, 2H, NCHC*H*$_2$), 2.38 and 2.34 (2m, 1H, NC*H*CH_2), 1.84 and 1.76 (2m, 1H, C*H*Me_2), 1.70–1.26 (4m, 2H, C*H*$_2$Me), 1.26, 1.16, 1.10 and 0.98 (4s, 6H, EtC*Me*$_2$), 1.01, 0.93, 0.87 and 0.65 (4d, *J*=6.6 Hz, CH*Me*$_2$), 0.92 and 0.87 (2t, 3H, CH_2*Me*) ppm. $C_{19}H_{31}F_6N_2PdSb$ requires: C, 36.24; H, 4.96; N, 4.45%. Found: C, 36.26; H, 4.98; N, 4.46.

*3.5.1. Crystallography of **9***

Monoclinic, space group $P2_1$ (No. 4), *a*=8.742(7), *b*=14.621(9), *c*=9.744(7) Å, β=113.01(5)°, *Z*=2, *V*=1146(2) Å^3, d_{calc}=1.743 Mg m^{-3}, μ=2.013 mm^{-1}. The diffraction experiments were carried out at 200 K on a fully automated CAD4 diffractometer using graphite-monochromated Mo-Kα radiation (λ=0.71069 Å). 3443 independent reflections were collected, 3421 observed for $I>2\sigma(I)$. Final *R* factors: R_1=0.0470, wR_2=0.1337. Intensity data corrected for Lorentz, polarisation and absorption effects, no decay. The structure was solved by direct methods using SIR97[19] and refined by full matrix least-squares calculations. The hydrogen atoms of the methyl groups and the aromatic hydrogens were experimentally located but placed in calculated positions. Orientational disorder of the allyl group was detected and the site occupation factor was refined for the central carbons, yielding the values 0.75 and 0.25. The SbF_6^- anion was found disordered over two orientations yielding two distinct F_6 octahedra around the Sb centre (0.55 and 0.45 occupation factors, respectively). The absolute configuration was determined and found in accord with the known configurations. The final refinement on F^2 proceeded by full-matrix least-squares calculations (SHELXL 93)[20] using anisotropic thermal parameters for all the non-hydrogen atoms.

*3.6. Enantioselective palladium-catalysed allylic alkylation. Preparation of **2***

A solution of sodium dimethyl malonate, generated from dimethyl malonate (0.396 g, 3 mmol) and NaH (0.072 g, 3 mmol), in dry THF (5 ml) was added dropwise to a stirred solution of 1,3-diphenyl-2-propenyl acetate (0.500 g, 2 mmol) and the palladium salt **9** (0.120 g, 0.2 mmol) in THF (5 ml) under Ar. The mixture was stirred for 36 h, whereupon the yellowish solution turned to orange, then green, and 1N HCl (5 ml) was added. The mixture was extracted with Et_2O (3×10 ml), the organic phase was dried (Na_2SO_4) and evaporated. Chromatography of the residue on a SiO_2 column eluting with cyclohexane:ethyl acetate (15:1) afforded the product **2**: 0.486 g, 50%; $[\alpha]_D^{25}$ +8.4 (*c* 0.62, $CHCl_3$); the e.e. 41% was determined by HPLC analysis (Daicel Chiralcel™ OD column, *n*-hexane:*i*-PrOH 99:1, flow rate 0.5 ml/min, retention times for the enantiomers: 21.15 and 22.22 min).

Acknowledgements

Financial support from the Ministero dell'Università e della Ricerca Scientifica e Tecnologica, Roma, and the University of Bologna (National Project 'Stereoselezione in Sintesi Organica. Metodologie ed Applicazioni') is gratefully acknowledged.

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