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Synthesis and resolution of 2-(2-diphenylphosphinyl-naphthalen-1-yl)-1-isopropyl-1*H*-benzoimidazole; a new atropisomeric *P*,*N*-chelating ligand for asymmetric catalysis

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Abstract—A multistep synthesis resulting in a good yield of the title compound **13** (BIMNAP) has been developed based on *N*,*N*-acetal-formation and oxidation with MnO_2. The product **11** is converted into the corresponding trifluoromethane sulfonate **12** by treatment with $(CF_3SO_2)_2O$ followed by a nickel-catalysed coupling-reaction with $HPPh_2$. Resolution of the phosphanamine **13** was carried out via fractional crystallisation of the diastereomeric hexafluorophosphate salts of the Pd-complex **15**, formed from reaction of **13** with (+)-di-μ-chlorobis{2-[1-(dimethylamino)ethyl]phenyl-C,N}dipalladium (*S*)-**14**. The absolute configurations of the two diastereomers were determined by X-ray crystallography.

1. Introduction

Of the many types of ligands which could be used for catalytic asymmetric reactions, chiral tertiary phosphines have been established as the most effective for homogeneous transition metal catalysis.[1,2] Due to the success of the DIOP-ligand developed by Kagan, C_2-symmetric bisphosphine ligands dominated asymmetric catalysis for a long time.[3] One of the most effective chiral bisphosphine ligands proved to be atropisomeric BINAP,[4] which was introduced by Noyori in the early 1980s and has proved highly successful in many asymmetric reactions including the synthetically important rhodium- and ruthenium-catalysed hydrogenation, hydroboration and hydroformylation protocols (Fig. 1).

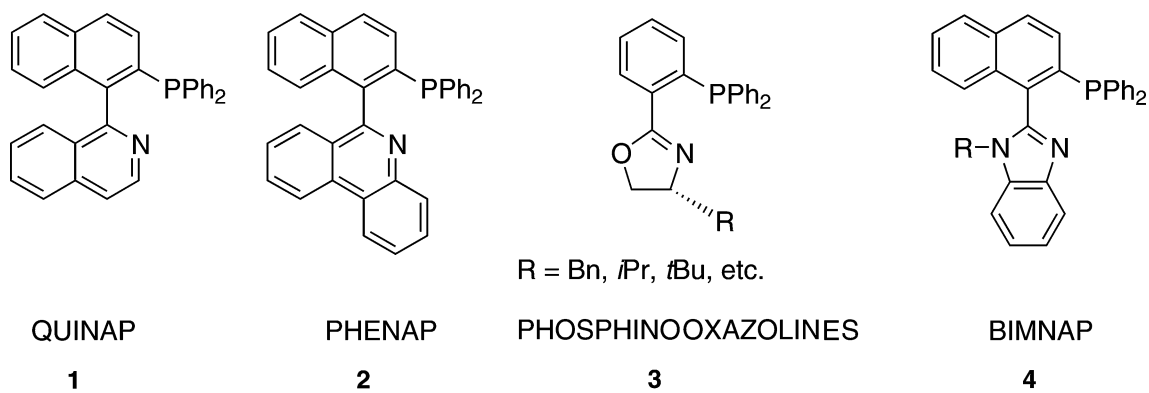

Figure 1.

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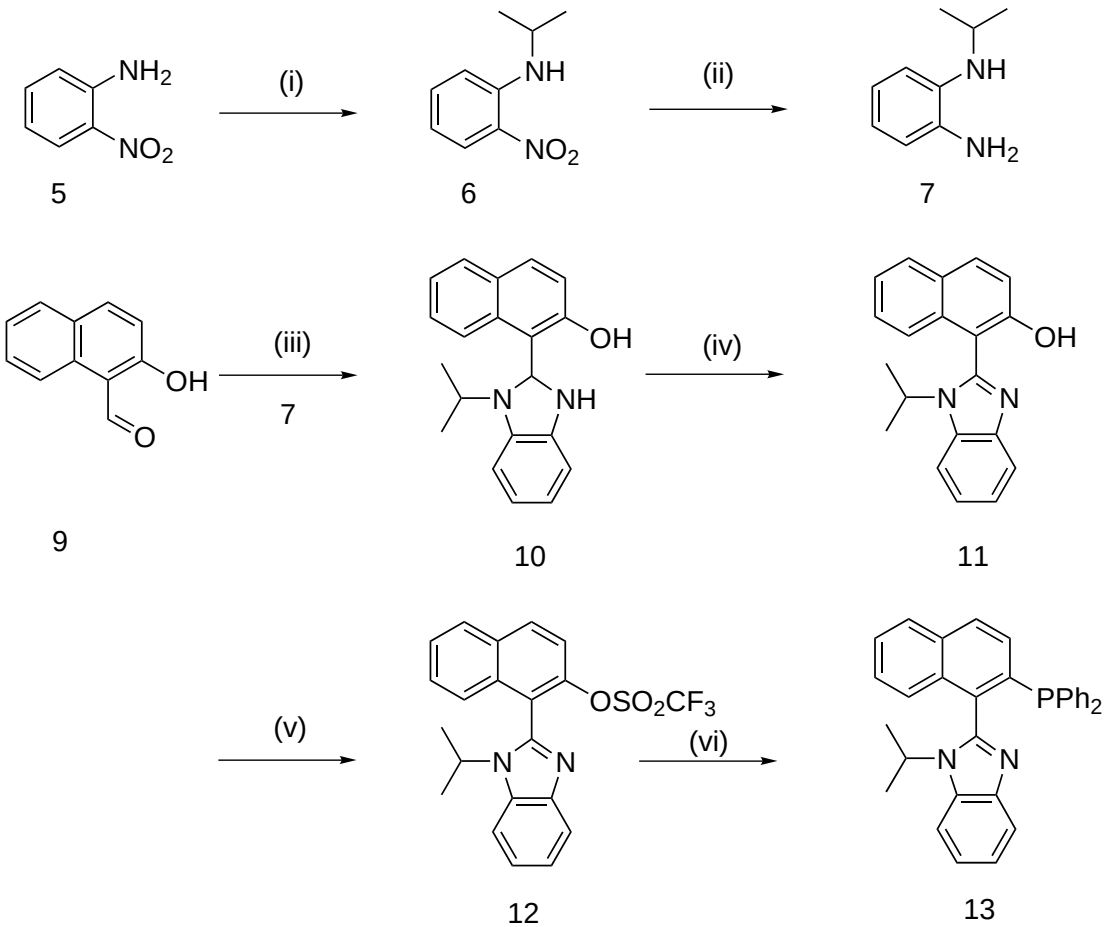
Subsequently, some monophosphine systems bearing an additional donor atom have been shown to be very effective ligands for chiral catalysis. Besides *O*-*P*-ligands, their *N*-*P* counterparts have attracted great interest. These include not only atropisomers like QUINAP **1** and PHENAP **2**, which have been used successfully in the rhodium-catalysed hydroboration of styrene and palladium-catalysed allylic substitution reaction,[5,6] but also simple phosphinooxazoline ligands **3** which were introduced by Helmchen,[7] Pfaltz[8] and Williams.[9] Phosphinoxazoline ligands induce excellent enantio-selectivities in palladium-catalysed allylic alkylations with 1,3-diphenylallyl acetate and other symmetrically substituted allyl derivatives. We wondered if related *P*-*N*-systems of the type **4** could be developed, which by proper choice of R group could lead to atropisomers sufficiently stable to be resolved and used as chiral ligands in asymmetric synthesis.

2. Ligand preparation

The synthesis of the new ligand **13** started with *N*,*N*-acetal formation of the diamine **7** and the aldehyde **9** to give the 2,3-dihydro-1*H*-benzoimidazole **10** followed by oxidation to the 1*H*-benzoimidazole system **11** (Scheme 1).

The diamine **7** could be prepared easily from 2-nitrophenylamine **5** by reductive amination with acetone/$BH_3{\cdot}SMe_2$[10] to give **6** in 92% yield followed by reduction of the nitro-group with H_2 over Pd/C in EtOH (98% yield).[10,11] Heating **7** and the commercially available aldehyde **9** for 2 h in refluxing MeOH then gave the *N*,*N*-acetal **10** in 63% yield. On dehydration of **10** with MnO_2 in benzene the product **11** was formed and precipitated due to its rather poor solubility in benzene. The residue after filtration of the reaction mixture had to be extracted with hot DMF to give **11** in 55% yield. Treatment of the naphthol system **11** with trifluoromethanesulfonic anhydride in the presence of 4-(*N*,*N*-dimethylamino)pyridine gave the corresponding trifluoromethanesulfonate **12** (94% yield), the electrophilic component for the final C–P coupling reaction. Ni(dppe)Cl_2 catalysed this reaction to afford the target molecule **13** in 50% yield.[12] As expected this molecule proved to be atropisomeric, as evidenced by the appearance of two doublets in the ^1H NMR spectrum for the two diastereotopic methyl groups and additionally shown by the fact that on a chiral LC-column (Chiracel OD) two peaks were observed, indicating two enantiomers.



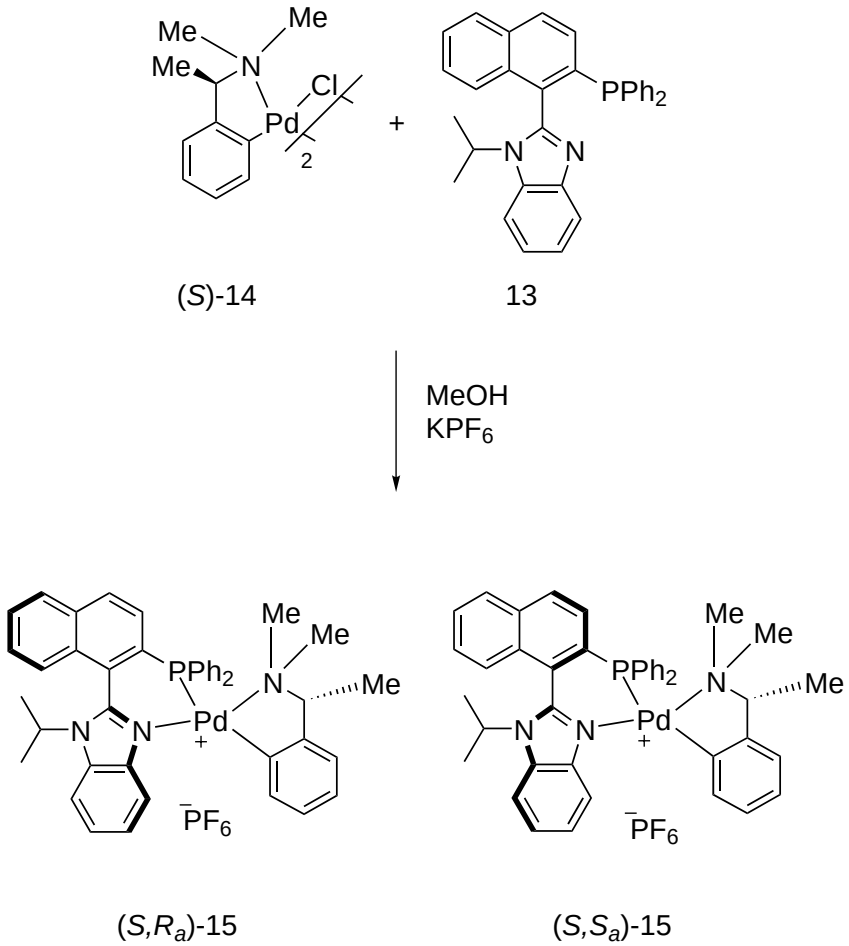
Scheme 1. *Reagents and conditions*: (i) $(CH_3)_2CO$, $BH_3S{\cdot}Me_2$, NH_3; (ii) H_2, Pd/C, EtOH; (iii) MeOH, reflux; (iv) MnO_2, benzene, reflux; (v) $(CF_3SO_2)_2O$, 4-DMAP, CH_2Cl_2; (vi) Ni(dppe)Cl_2, $HPPh_2$, DABCO, DMF, 90°C.

3. Ligand resolution

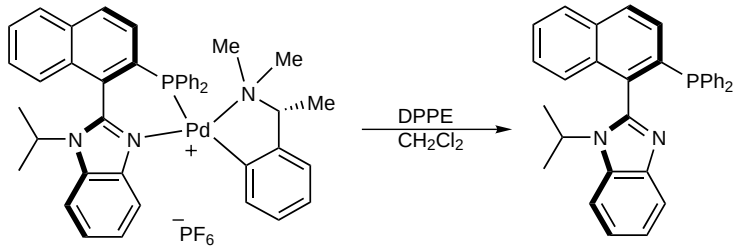
The resolution of bidentate *P*,*N*-ligands has been widely studied and *ortho*-palladated derivatives of (*S*)-dimethyl(1-phenylethyl)amine have proved to be useful resolving agents.[13] The phosphinamine **13** and (*S*)-**14** were stirred in methanol for 2 h; on addition of KPF_6 the diastereomeric products (S,R_a)-**15** and (S,S_a)-**15** precipitated and could be isolated after filtration as a pale yellow solid, which was shown by ^{1}H NMR to consist of a 1:1 mixture of diastereomers (Scheme 2).

The key resonances which confirm this are associated with the benzylic methine protons, which for one diastereomer appear as a quintet at 4.82 ppm and for the other at 3.55 ppm. The ^{31}P NMR spectrum exhibits two peaks, one at 38.6 ppm and the other at 39.1 ppm again integrating to a 1:1 mixture. The diastereomeric pair could be separated by fractional crystallisation from CH_2Cl_2/Et_2O (1:1) to give diastereomerically pure (S,S_a)-**15** in 40% yield. On addition of ethanol the other diastereomer crystallised from the filtrate within a week. Once resolved, the free (S_a)-**13** ligand was generated by adding 1,2-bis(di-phenylphosphino)ethane to (S,S_a)-**15** in dichloromethane at ambient temperature over 24 h. The specific rotation of the free ligand (S_a)-**13** was found to be $[\alpha]_D^{20}$ −75. As the specific rotation value did not change after heating in refluxing 1,4-dioxan solution for several hours, racemisation of (Sa)-**13** seems to be slow below 100°C (Scheme 3).

The absolute configurations of the two diastereomeric salts **15** were determined by X-ray diffraction, and important bond distances, angles and torsion angles are listed in Table 1. The X-ray structures of the cations, which emphasise the enantiomeric relationship between the phosphinamine ligands in these structures, are displayed in Figs. 2a and 2b. Inspection of Fig. 2a shows that the axial chirality of the atropisomeric ligand is S_a, whereas the R_a configuration is found for this ligand shown in Fig. 2b. While the N(1)–C(2)–C(13)–C(14) torsion angles of 52.3(8) and −49.6(8)° in these two ligands necessarily differ in sign, their magnitudes are essentially identical. Markedly smaller absolute values for these torsion angles appear to be prohibited by the non-bonded contacts between the isopropyl and the naphthalenyl groups. The chelate ligands coordinate to the Pd atoms in a distorted square-planar fashion—the rms deviation of the ligating atoms from planarity is slightly larger for the (S,S_a)-isomer, 0.193 Å, than for the (S,R_a)-derivative, 0.162 Å. The P(1)–Pd–N(1) angle of the (S,S_a)-**15** complex is barely smaller than that of (S,R_a)-**15**, and a similar chelate bite, 82.2(1)°, was found for the corresponding QUINAP derivative.[14]



Scheme 2.



(S,S_a)-15 (S_a)-13

Scheme 3.

Due mainly to the torsion about the C(2)–C(13) bonds in **15**, the Pd and P(1) atoms deviate by nearly 0.6 Å to opposite sides of the planes defined by the Pd–N(1)–C(2)–C(13)–C(14)–P(1) chelate rings, and Cremer–Pople analyses[15] of their ring puckering indicates that both rings exhibit a conformation which lies between canonical *half-chair* and *twist-boat* forms. The helicities of these chelate rings as determined by the signs of the P(1)–Pd–N(1)–C(2) torsion angles are *M* and *P* for the (S,S_a)- and (S,R_a)-derivatives, respectively. Another feature associated with the axial chirality of the phosphinamine ligands is the propeller-like arrangement of the aryl groups around the P(1) atoms. A right-handed propeller is found for (S,S_a)-**15**, while that of (S,R_a)-**15** is left-handed. The close correlation of the magnitude of torsion angles such as Pd–P(1)–C(14)–C(15) (Table 1) suggests a degree of rigidity for the propellers. This might arise not only from an interlocking of the aryl substituents, but also from the quasi-parallel orientation of the phenyl group C(23)–C(28) and the benzoimidazole system. Both chelate rings formed with the phenylethylamine ligands exhibit envelope conformations with the flap atoms N(4) deviating from the planes defined by the other four atoms by 0.718(5) and 0.835(6) Å in (S,S_a)-**15** and (S,R_a)-**15**, respectively. The helicities of these heterocycles, as determined from the sign of the N(4)–Pd–C(35)–C(40) torsion angles (Table 1), are *M* in (S,S_a)-**15** and *P* in (S,R_a)-**15**. To this extent, the configurations of these rings are in an enantiomeric relationship, but true enantiomerism is prohibited by the (*S*)-configuration of each ring atom C(41). Inspection of models with this chirality for the methine carbon shows that changing the helicity of the five-membered ring from *M* to *P* forces the methyl group C(42) to flip from the equatorial position in (S,S_a)-**15** to the axial position in (S,R_a)-**15**.

Thus, the helicities of the phenylethylamine chelate rings and the chirality of the phosphinamine ligands are interdependent. The NMR spectra show that these conformations are retained in solution. Especially indicative are the benzylic ^{13}C-chemical shifts with 25.23 ppm for the axial methyl group in (S,R_a)-**15** and 9.04 ppm for the equatorial methyl group in (S,S_a)-**15**; Furthermore, a ^{31}P coupling of 6 Hz to the benzylic CH is found in (S,R_a)-**15**, whereas in (S,S_a)-**15**, with an axially oriented CH, no such coupling is observed. This is in full accord with the corresponding values in similar systems.[14] A likely mechanism for the exchange of chiral structural features between the ligands might involve repulsions between the aryl group C(35)→C(40) and the phosphine-bonded phenyl group C(29)→C(34), which also lies in the Pd coordination plane. Clearly the sense of rotation of the former group about the Pd–C(35) bond with respect to the Pd–N(4) linkage will reflect the disposition of the phosphine substituent. Occurrences of axial and equatorial substitution of the phenylethylamine chelate rings are well known, and an interesting example of axial/equatorial disorder was reported when two (*S*)-phenylethylamine ligands were related by an inversion centre—which inverted the helicity of the chelate rings.[14] The present study underscores how the interplay of phosphinamine chirality and various ligand helicities eventually affects the conformation of other ligands in the Pd coordination sphere.

The application of transition metal complexes of this new ligand in catalytic asymmetric synthesis will form the subject of future publications from this group.

Table 1. Selected bond lengths (Å) and angles (°) in (S,S_a)-**15** and (S,R_a)-**15**

	(S,S_a)-**15**	(S,R_a)-**15**
Pd–P(1)	2.247(2)	2.240(1)
Pd–N(1)	2.151(4)	2.117(4)
Pd–N(4)	2.134(5)	2.156(5)
Pd–C(35)	1.997(7)	1.986(6)
P(1)–Pd–N(1)	80.6(1)	82.4(1)
N(4)–Pd–C(35)	81.4(2)	80.5(2)
P(1)–Pd–C(35)	101.2(2)	98.4(2)
N(1)–Pd–N(4)	98.3(2)	98.8(2)
N(1)–C(2)–C(13)–C(14)	52.3(8)	−49.6(8)
P(1)–Pd–N(1)–C(2)	−49.0(5)	45.3(5)
Pd–P(1)–C(14)–C(15)	125.5(6)	−123.6(5)
Pd–P(1)–C(23)–C(28)	138.2(6)	−142.2(5)
Pd–P(1)–C(29)–C(34)	128.3(7)	−128.6(5)
N(4)–Pd–C(35)–C(40)	−16.9(5)	23.0(6)

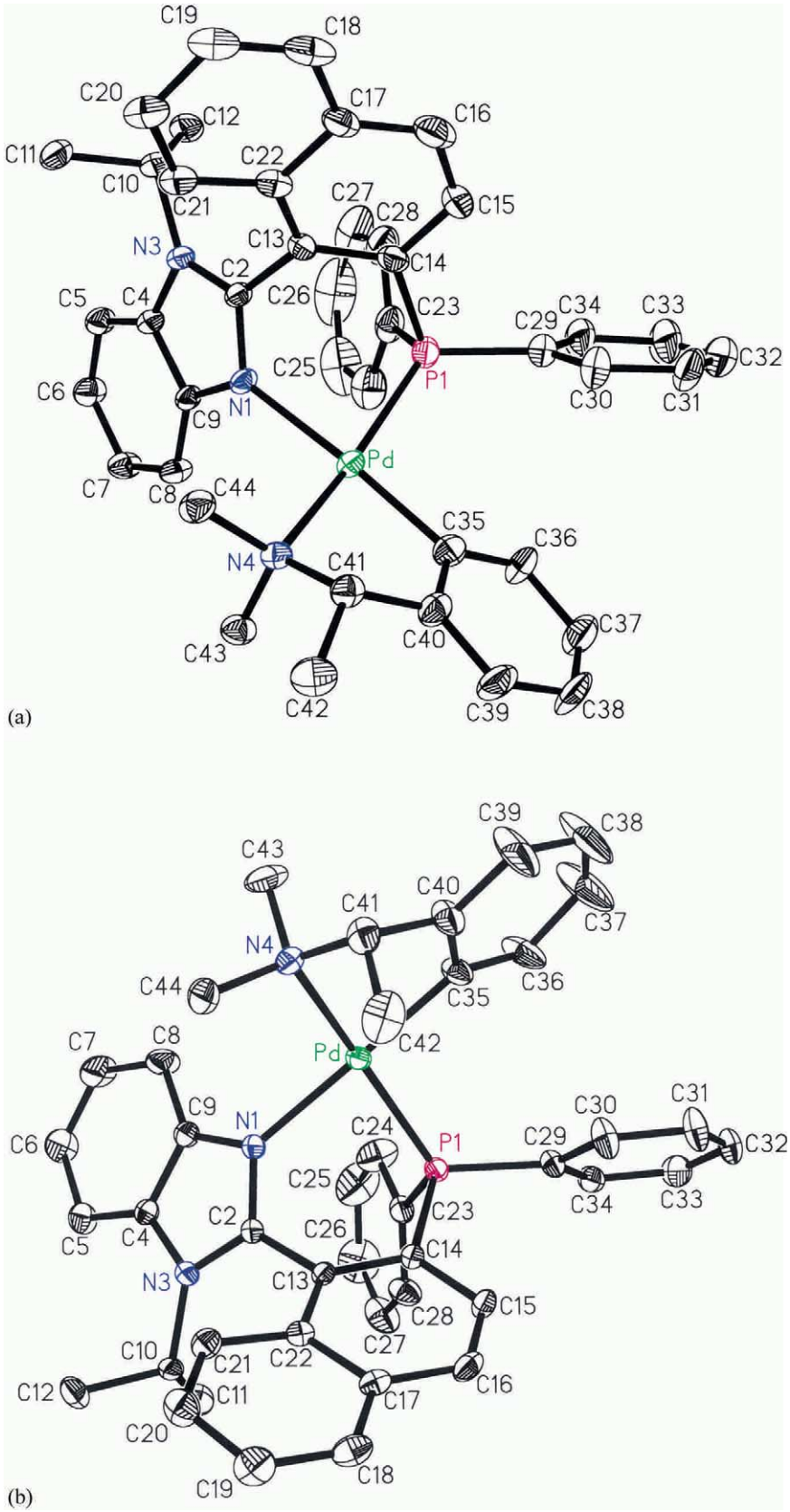


Figure 2. Perspective drawing of (S,S_a)-**15** (a) and (S,R_a)-**15** (b) with 20% probability thermal ellipsoids and hydrogen atoms omitted for the sake of clarity.

4. Experimental

4.1. Apparatus and materials

NMR spectra were recorded on a Bruker ARX 400 spectrometer. ^{1}H and ^{13}C chemical shifts are reported in δ ppm relative to the used deuterosolvent. ^{31}P chemical shifts are reported relative to 85% aqueous phosphoric acid (0 ppm). Mass spectra were recorded on a Varian MAT 311A. EI-HR-MS were recorded on a MAT 95 (Fa. Finnigan), ESI-HR-MS on a LCT (Fa. Micro Mass). IR spectra were recorded on a Nicolet Avatar 360 FT spectrometer. Optical rotations were recorded on a Perkin–Elmer 241 polarimeter. Melting points were recorded on a Gallenkamp MFB-595 and are uncorrected. Solvents were dried immediately before use by distillation from standard drying agents. DMF (Aldrich) was degassed and purged with argon three times before use. Separations by column chromatography were performed using Merck Kieselgel 60. All used chemicals were commercially available. For ease of interpretation of NMR data the numbering scheme in Fig. 3 is used for ligand **4** and related compounds are numbered similarly.

4.2. Procedures

4.2.1. Synthesis of isopropyl-(2-nitrophenyl)amine 6. 2-Nitrophenylamine **5** (10 g, 72.4 mmol) was dissolved in CH_2Cl_2 (60 mL) and HOAc (30 mL). Acetone (12.6 g, 16 mL, 218 mmol) was added and the solution stirred for 5 min. After cooling to 0°C $BH_3{\cdot}SMe_2$ (10 M in CH_2Cl_2, 8.6 mL, 86 mmol) was added slowly. After stirring the mixture at room temperature for 24 h the pH was adjusted to 8 by adding aqueous NH_3 solution. After separating the layers and washing twice with CH_2Cl_2 the organic extracts were combined and dried over sodium sulphate. Removing the solvent in vacuo gave an oil which was stirred in Et_2O and filtered. The organic layer was washed with brine, dried over sodium sulphate and the solvent was removed in vacuo to afford isopropyl-(2-nitrophenyl)amine **6** as an orange oil. (12 g, 92%) ^{1}H NMR (400 MHz): δ ($CDCl_3$) 8.12 (d, 1H, $J=8.6$ Hz, H_5), 7.96 (s, 1H, NH), 7.38 (m, 1H, H_7), 6.83 (d, 1H, $J=8.7$ Hz, H_6), 6.56 (m, 1H, H_8), 3.80 (sept, 1H, $J=8.6$ Hz, H_{10}), 1.30 (d, 6H, $J=6.4$ Hz, CH_3); ^{13}C NMR (100 MHz): δ ($CDCl_3$) 144.7 (C_9), 136.0 (C_7), 131.7 (C_4), 126.9 (C_5), 114.7 (C_6), 43.7 (C_{10}), 22.6 (CH_3); m/z (EI-MS 70 eV) 180 (M, 100%), 165 (81); EI-HR-MS: requires 180.0899, found 180.0902; ν_{max} (Neat) 3380 (NH_2), 3100 (Ar-H), 1350 (Ar-NO_2).

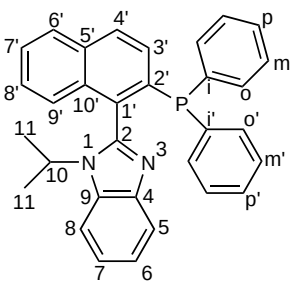


Figure 3.

4.2.2. Synthesis of (*N*-isopropyl)benzene-1,2-diamine 7. 2-Nitrophenylamine **6** (12 g, 66.6 mmol) was dissolved in EtOH (200 mL). Pd/C was added and the suspension was hydrogenated at room temperature for 12 h at atmospheric pressure. After the filtration of the catalyst the filtrate was condensed under reduced pressure to give *N*-isopropyl-benzene-1,2-diamine **7** as a black oil. (9.8 g, 98%) ^{1}H NMR (400 MHz): δ ($CDCl_3$) 6.86 (m, 1H, H_7), 6.70 (m, 3H, $H_5+H_6+H_8$), 3.64 (sept, 1H, $J=6.8$ Hz, H_{10}), 3.25 (s, 3H, NH+NH_2), 1.28 (d, 6H, $J=6.8$ Hz, H_{11}); ^{13}C NMR (100 MHz): δ ($CDCl_3$) 136.8 (C_4), 134.4 (C_9), 120.5 (C_7), 118.3 (C_6), 116.7 (C_5), 112.8 (C_8), 44.1 (C_{10}), 23.1 (C_{11}); m/z (EI-MS 70 eV) 150 (M^+, 100%), 135 (37), 107 (14), 92 (28), 80 (17), 58 (6); ν_{max} (Neat) 3369 (NH_2), 2970 (Ar-H), 1616, 1572, 1511, 1418, 1350, 1268, 1237, 1171, 741.

4.2.3. Synthesis of 1-(1-isopropyl-2,3-dihydro-1*H*-benzoimidazol-2-yl)naphthalen-2-ol 10. To a solution of 2-(isopropylamino)phenylamine **7** (9.8g, 65.2%) in MeOH (100 mL) was added a solution of 2-hydroxy-naphthalene-1-carbaldehyde **9** (11.2 g, 65.9 mmol) in MeOH (30 mL). The solution was heated under reflux for 60 min. The suspension was then allowed to cool to room temperature and the solid was filtered off. The solid was washed with MeOH and dried to afford 1-(1-isopropyl-2,3-dihydro-1*H*-benzoimidazol-2-yl)naphthalen-2-ol **10** as a red solid (12.7g, 63%) mp 107°C, ^{1}H NMR (400 MHz): δ ($CDCl_3$) 9.46 (s, 1H, H_2), 8.19 (d, 1H, $J=8.5$ Hz, $H_{6'}$), 7.86 (d, 1H, $J=9.0$ Hz, $H_{4'}$), 7.79 (d, 1H, $J=8.1$ Hz, $H_{9'}$), 7.56 (m, 1H, $H_{7'}$), 7.39 (m, 1H, $H_{8'}$), 7.22 (m, 2H, $H_{3'}+H_5$), 7.14 (m, 1H, H_8), 6.78 (m, 2H, H_6+H_7), 4.27 (s, 1H, NH), 3.76 (sept, 1H, $J=6.3$ Hz, H_{10}), 1.32 (d, 6H, $J=6.3$ Hz, CH_3); ^{13}C NMR (100 MHz): δ ($CDCl_3$) 164.4 ($C_{2'}$), 157.3 (C_2), 141.2, 134.4 (C_4+C_9), 135.2 ($C_{4'}$), 132.7 ($C_{10'}$), 129.2 ($C_{9'}$), 128.2, 120.1 ($C_{3'}+C_5$), 127.9 ($C_{7'}$), 127.7 ($C_{5'}$), 123.5 ($C_{8'}$), 119.3 ($C_{6'}$), 118.7 (C_8), 116.6 (C_7), 111.4 (C_6), 109.9 ($C_{1'}$), 44.2 (C_{10}), 23.0 (C_{11}); EI-HR-MS: requires 302.1419, found 302.1420; ν_{max} (KBr) 3440 (OH, NH), 2966 (CH), 1623 (Ar), 1577 (Ar).

4.2.4. Synthesis of 1-(1-isopropyl-1*H*-benzoimidazol-2-yl)naphthalen-2-ol 11. To a solution of 1-(1-isopropyl-2,3-dihydro-1*H*-benzoimidazol-2-yl)naphthalen-2-ol **10** (10.0 g, 32.9 mmol) in benzene (250 mL) was added freshly activated MnO_2 (10.3g, 119 mmol) and the mixture was heated under reflux for 12 h. The suspension was allowed to cool to room temperature and the solid was filtered off. The filtrate was extracted three times with hot *N*,*N*-dimethylformamide and the solvent was removed in vacuo to give 1-(1-isopropyl-1*H*-benzoimidazol-2-yl)-naphthalen-2-ol **11** as a grey powder. (5.5g, 55%); mp >200°C; ^{1}H NMR (400 MHz): δ (D_7-DMF) 10.3 (s, 1H, OH), 7.93 (d, 1H, $H_{6'}$), (7.84, d, 1H, $H_{4'}$), 7.77 (d, 1H, $H_{9'}$), 7.67 (d, 1H, H_8), 7.2 (m, 5H, $H_{3'}+H_{7'}+H_{8'}+H_6+H_7$), 7.08 (d, 1H, H_5), 4.21 (sept, 1H, $J=6.9$ Hz, H_{10}), 1.44 (dd, 6H, $J=6.9$ Hz, H_{20}); ^{13}C NMR (100 MHz): δ (D_7-DMF) 154.5 ($C_{2'}$), 149.2 (C_2), 143.9, 134.0 (C_4+C_9), 132.9 ($C_{10'}$), 131.2 ($C_{6'}$), 127.9 ($C_{4'}$), 127.5 ($C_{5'}$), 123.5 (C_5), 119.3 (C_8), 126.9, 123.0,

121.6, 121.0, 118.0 ($C_{3'}$+$C_{7'}$+$C_{8'}$+C_6+C_7), 112.1 ($C_{9'}$), 110.2 ($C_{1'}$), 48.3 (C_{10}), 21.2, 20.7 (C_{11}); *m*/*z* (EI-MS 70 eV) 302 (M^+, 100%), 286 (57), 259 (70), 231 (43), 77 (22), 66 (23), 43 (20); EI-HR-MS: requires 302.1419, found 302.1818; ν_{max} 3427 (OH), 2968–2870 (Ar-H), 1626 (Ar).

4.2.5. Synthesis of give trifluoromethanesulfonic acid 1-(1-isopropyl-1*H*-benzoimidazol-2-yl)naphthalen-2-yl-ester 12. 1-(1-Isopropyl-1*H*-benzoimidazol-2-yl)naphthalen-2-ol **11** (2.0 g, 6.6 mmol) was suspended in CH_2Cl_2 (20 mL) and 4-dimethylaminopyridine (2.42 g, 20.0 mmol) was added. Trifluoromethanesulphonic anhydride (2.8 g, 1.7 mL, 9.9 mmol) was cautiously added via syringe and the solution was then stirred at room temperature for about 2 h. Thereafter the solution was washed with 1 M hydrochloric acid (3×50 mL), water (1×50 mL) and saturated brine (1×50 mL). After drying the solution with sodium sulphate the solvent was removed in vacuo to give trifluoro-methanesulfonic acid 1-(1-isopropyl-1*H*-benzoimidazol-2-yl)naphthalen-2-yl-ester **12** as a beige foam (2.8 g, 94%) ^{1}H NMR (400 MHz): δ ($CDCl_3$) 8.26 (d, 1H, H_8), 8.16 (m, 1H, H_5), 8.04 (d, 1H, $H_{6'}$), 7.90 (m, 1H, $H_{4'}$), 7.70–7.60 (m, 5H, H_7+H_6+$H_{9'}$+$H_{8'}$+$H_{7'}$), 7.35 (m, 1H, $H_{3'}$), 4.28 (sept, 1H, H_{10}), 1.61 (dd, 6H, J=6.9 Hz, H_{11}); ^{13}C NMR (100 MHz): δ ($CDCl_3$) 146.0 ($C_{2'}$), 145.2, 144.2 (C_4+C_9), 133.6 (C_2), 133.0, 132.2 ($C_{5'}$+$C_{10'}$), 132.6, 128.3 ($C_{6'}$+$C_{9'}$), 128.5, 126.10 ($C_{3'}$+$C_{4'}$), 122.9, 122.2 (C_5+C_8), 119.9 ($C_{1'}$), 127.6, 119.0 ($C_{7'}$+$C_{8'}$), 116.7 (CF_3), 112.2, 120.8 (C_6+C_7), 49.5 (C_{10}), 21.1, 21.8 (C_{11}); *m*/*z* (EI-MS 70 eV) 434 (M^+, 95%), 301 (100), 285 (38), 259 (97), 231 (76), 77 (30), 43 (25); EI-HR-MS: requires 434.0912, found 434.0916; ν_{max} (KBr) 3448, 3062 (Ar-H), 2942 (aliph.).

4.2.6. Synthesis of 2-(2-diphenylphosphanyl-naphthalen-1-yl)-isopropyl-1*H*-benzimidazole 13. A solution of Ni(dppe)Cl_2 (313.8 mg, 0.58 mmol) and diphenylphosphine (548 mg, 2.94 mmol, 510 μl) in DMF (25 mL) was heated to 90°C. A solution of trifluoromethanesulfonic acid 1-(1-isopropyl-1*H*-benzoimidazol-2-yl)-naphthalen-2-yl-ester **12** (2.65g, 5.88 mmol) and DABCO (2.63 g, 23.5 mmol) in DMF (25 mL) was added via syringe. After 1 h of heating another 510 μl diphenylphosphane was added. The dark green solution was stirred for 6 h. Then the solvent was removed in vacuo. The green foam was purified by column chromatography (toluene/ethylacetate 5:1) to give 2-(2-diphenylphosphanyl-naphthalen-1-yl)-isopropyl-1*H*-benzimidazole **13** as an off white solid (1.1 g, 40%) mp 82°C; ^{1}H NMR (400 MHz): δ ($CDCl_3$) 7.9–7.8 (m, 3H, $H_{6'}$+$H_{9'}$+$H_{6/7}$), 7.66 (dd, 1H, J=6.0 Hz, J=3.2 Hz, $H_{6/7}$), 7.51 (m, 1H, $H_{7'/8'}$), 7.3–7.2 (m, 14H, $H_{3'}$+$H_{4'}$+H_5+H_8+H_o+$H_{o'}$+H_m+$H_{m'}$+H_p+$H_{p'}$), 4.20 (sept, 1H, J= 6.9 Hz, H_{10}), 1.44 (dd, 6H, J=6.9 Hz, H_{11}); ^{13}C NMR (100 MHz): δ ($CDCl_3$) 151.5 ($C_{2'}$), 144.2 (C_2), 137.6, 137.4 (C_4+C_9), 136.8 ($C_{10'}$+C_i+$C_{i'}$), 133.4 ($C_{5'}$), 132.7 ($C_{1'}$), 130.0 ($C_{3'/p/p'}$), 133.4, 133.3, 128.6, 128.5, 128.4, 128.3 (C_o+$C_{o'}$+C_m+$C_{m'}$), 127.3, 127.1 ($C_{7'}$+$C_{8'}$), 126.1 ($C_{3'/p/p'}$), 133.1, 122.2, 121.7 ($C_{4'}$+C_5+C_8), 129.9, 128.0, 120.7, 112.1 ($C_{6'}$+$C_{9'}$+C_6+C_7), 49.2 (C_{10}), 21.7, 21.1 (C_{11}); *m*/*z* (EI-MS 70 eV) 470 (M^+, 15%), 427 (100), 351 (25), 273 (50), 213 (50); EI-HR-MS: requires 486.1861, found 486.1844; ν_{max} (neat) 3050 (Ar-H), 2970 (CH aliph.), 1450 (C-P).

4.2.7. Resolution of 2-(2-diphenylphosphanyl-naphthalen-1-yl)-isopropyl-1*H*-benzo-imidazole (*RS*)-13: formation of diastereomers (*S*,*S*)-15 and (*S*,*R*)-15. (+)-Di-μ-chloro-bis{2-[1-(dimethylamino)ethyl]phenyl-*C*,*N*}-dipalladium (*S*)-**14** (222 mg, 0.382 mmol) and 2-(2-diphenylphosphanyl-naphthalen-1-yl)-isopropyl-1*H*-benzo-imidazole **13** (360 mg, 0.765 mmol) were placed in a Schlenk tube under argon. Degassed methanol (22 mL) was added via a syringe. The mixture was stirred until the solids had dissolved to give a pale yellow solution. Potassium hexafluorophosphate (140 mg, 0.76 mmol) in water (25 mL) was added with vigorous stirring and a pale green/yellow solid precipitated. The solid was collected by filtration and washed with ether to give a 1:1 mixture of (S,S_a)-**15** and (S,R_a)-**15** as a pale yellow solid (520 mg, 80%) mp >200°C; crystallisation of the racemic mixture from CH_2Cl_2/Et_2O (1/1) gave (S,S_a)-**15**. $[\alpha]_D^{20}$ −386 (*c*= 0.5, CH_2Cl_2), ^{1}H NMR (400 MHz): δ ($CDCl_3$): 8.12 (m, 3H), 7.76 (m, 3H), 7.59–7.43 (m, 6H), 7.35–7.27 (m, 4H), 7.14 (s, 2H), 7.03–6.98 (m, 2H), 6.89 (m, 1H), 6.80 (d, 1H), 6.43 (m, 1H), 6.08 (m, 1H), 4.82 (m, benzylic-H), 3.88 (m, 1H, H_{10}), 2.81 (d, 3H, N-CH_3), 2.69 (d, 3H, N-CH_3), 1.68 (d, 3H, H_{11}), 1.36 (d, 3H, benzylic-CH_3), 0.59 (d, 3H, H_{11}); ^{31}P NMR (161.9 MHz): δ ($CDCl_3$): 39.14, 143.14 (PF_6^-); *m*/*z* (EI-MS 70 eV); ESI-HR-MS: requires 720.2088, found 720.2085; ν_{max} (KBr) (mixture) 3440, 3056. 2985, 1635, 1456, 1437, 1406, 1101, 840, 747, 557.

4.2.8. (*S*)-2-(2-Diphenylphosphanyl-naphthalen-1-yl)-isopropyl-1*H*-benzimidazole 13. 1,2-Bis(diphenylphosphino)ethane (0.247 g, 0.62 mmol) was added to a solution of (S,S_a)-**15** (0.270 g, 0.31 mmol) in dichloromethane (20 mL) and the resulting solution was stirred for 24 h. The solvent was removed in vacuo and the residue was purified by flash chromatography over a short column, eluting with toluene/ethyl acetate (5:1) to give (S_a)-2-(2-diphenylphosphanyl-naphthalen-1-yl)-isopropyl-1*H*-benz-imidazole **13** as a white solid. $[\alpha]_D^{20}$ −75 (*c*=0.5, CH_2Cl_2), identical in all other respects to the previously prepared racemic sample (*RS*)-**13**.

4.3. Crystal structure determinations of (S,S_a)-15 and (S,R_a)-15

Crystals were glued to glass fibres. X-Ray data were measured with a P3 diffractometer using Ni filtered Cu Kα radiation (λ 1.54184 Å). Intensities were registered with ω scans and corrected for absorption. The positions of the non-hydrogen atoms were determined conventionally and refined anisotropically while the hydrogen atoms were placed in idealised positions and assigned isotropic temperature factors. Crystal data are given in Table 2. Further crystallographic data, except for structure factors, have been deposited at the Cambridge Crystallographic Data Centre. The deposit numbers are CCDC 174211 and 174212 for (S,S_a)-**15** and (S,R_a)-**15**, respectively. Copies of the data can be

Table 2. Crystal data for (S,S_a)-**15** and (S,R_a)-**15**

	(S,S_a)-**15**	(S,R_a)-**15**
Empirical formula	$C_{42}H_{41}F_6N_3P_2Pd$	$C_{42}H_{41}F_6N_3P_2Pd$
Formula weight	870.12	870.12
Crystal system	Orthorhombic	Orthorhombic
Space group	$P2_12_12_1$	$P2_12_12_1$
a (Å)	11.2570(12)	11.0861(14)
b (Å)	11.7293(11)	17.040(2)
c (Å)	31.941(4)	21.517(3)
V (Å^3)	4217.4(8)	4064.6(8)
Z	4	4
D_{calcd} (g cm^{-3})	1.370	1.422
Theta range (°)	2.77–68.97	3.31–69.31
Limiting indices	$0\leq h\leq 13$	$0\leq h\leq 13$
	$0\leq k\leq 14$	$0\leq k\leq 20$
	$-38\leq l\leq 38$	$-26\leq l\leq 26$
Reflections collected	9110	8470
Unique	7855	7614
R(int)	0.0283	0.0574
Observed ($I>2\sigma$)	6618	6990
Crystal size (mm)	$0.48\times0.23\times0.16$	$0.51\times0.27\times0.21$
μ (mm^{-1})	4.768	4.947
Transmission	0.5580–0.2749	0.4653–0.2565
R_1 (all data)	0.0631	0.0672
wR_2 (all data)	0.1219	0.1734
Goodness-of-fit on F^2	1.020	1.062
Parameters	518	518
ΔF map (e Å^{-3})	0.441 to −0.848	0.739 to −1.190
Extinction coefficient	0.00018(3)	None
Absolute structure parameter	−0.022(11)	−0.003(13)

obtained free of charge from The Director, CCDC, 12 Union Road, Cambridge CD2 1EZ, UK (fax: +44-1223-336033; e-mail: deposit@ccdc.cam.ac.uk or http://www.ccdc.cam.ac.uk).

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