Contrasting Behaviour of Related Palladium Complex-derived Resolving Agents. 8-H Conformational Locking of the 1-Naphthyl Side-chain

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The X-ray crystal structures of palladium complexes **4** and **6** derived from (*R*)-*N*,*N*-dimethyl-1-(1-naphthyl)ethylamine and (*S*)-*N*,*N*-dimethyl-1-phenylethylamine, respectively, are reported; in the latter case two diastereoisomers differing both in the ligand configuration and the conformation of the *C*,*N*-chelate ring cocrystallise as a quasiracemate.

In previous papers[1–3] we reported the synthesis and resolution of ligand **1** [1-(2-diphenylphosphino-1-naphthyl) isoquindine, QUINAP] and its application to catalytic asymmetric hydroboration and allylic alkylation. Resolution was easily achieved with the chloropalladium complex of (*R*)-*N*,*N*-dimethyl-1-(1-naphthyl)ethylamine **2** but failed with the chloropalladium complex of (*S*)-*N*,*N*-dimethyl-1-phenylethylamine **3**. In the former case, the (*R*,*S*)-diastereoisomer **4** could be completely separated from the (*R*,*R*)-diastereoisomer **5** in a single crystallisation, and (*R*,*S*)-**4** was also formed preferentially with a deficiency of resolving agent **2**. Both complexes **2** and **3** are widely used for the resolution of chelating ligands, in an empirical manner.[4] This made the rationalisation of our results interesting, and further work permits a general explanation to be put forward.

In the first paper,[1] the X-ray structure of the Pd complex of the less stable (*R*,*R*)-diastereoisomer **5** was reported. The structure of the more stable (*S*,*R*)-complex **4**† has now been solved and is shown in Fig. 1.‡ In common with all recorded X-ray structures of Pd complexes derived from **2**, this possesses an axial benzylic methyl group.[5]

Crystalline material was obtained in attempts to resolve QUINAP **1** with the phenylethylamine complex **3**, however, the species formed **6** was a mixture of two diastereoisomers, as racemic **1** was recovered on decomposition. Specifically, the NMR spectra of **6** exhibited benzylic chemical shifts associated with two distinct compounds in 1 : 1 ratio; ^{1}H : C*H*Me δ 3.53(dq), 4.73(q), ^{13}C : CH*Me* δ 25.2, 9.2. In comparison, the naphthylethylamino complexes **4** and **5** exhibit C*H*Me resonances at δ 4.82(dq) and 4.61(dq) respectively, with both CH*Me* resonances at δ 24.2. For the phenylethylamino complexes **6** we attribute the first-cited shifts to the diastereoisomer **6a** which has an axial *C*-methyl group, based on the similarity of its ^{13}C chemical shift to that of **4** and **5**, and comparable ^{31}P coupling of 6 Hz to the benzylic CH; the *ca.* δ 1 difference in C*H*Me chemical shifts between **6a** and **4** or **5** is due to differential aromatic deshielding. The other diastereoisomer **6b**, shown to have the (*S*,*S*)-configuration by synthesis from enantiomerically pure components, possesses an equatorial benzylic methyl group, leading to the distinct ^{13}C chemical shift of δ 9.2 and the absence of benzylic CH–coupling to phosphorus. The existence of two diastereoisomeric complexes with very different NMR spectra has been also noted for the biaryl diphosphine complexes **7a**,**b**[6] and **8a**,**b**[7] derived from **3** and may be a general phenomenon in this series.[9] In accord with this interpretation, analysis of the available X-ray literature confirms that both equatorial and axial conformations of the benzylic methyl group are accessible in the phenylethylamino series. The majority of such complexes possess an axial benzylic methyl group[6] but several examples of equatorial geometry are also known.[6,7,10]

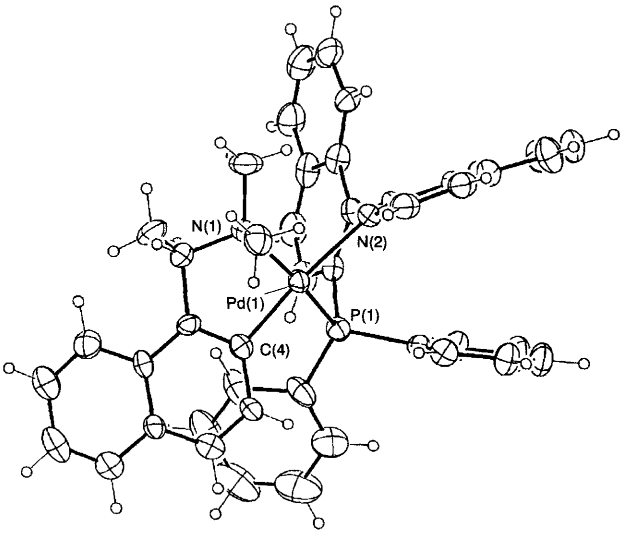
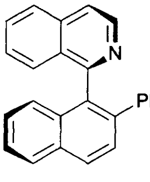
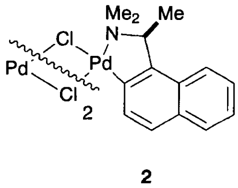


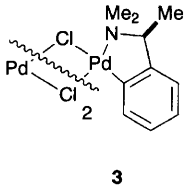
Fig. 1 Structure of complex **4**, the counterion and two CHCl$_3$ solvate molecules have been omitted for clarity. Selected bond lengths (Å) and angles (°): Pd(1)–P(1) 2.247(3), Pd(1)–N(1) 2.120(8), Pd(1)–N(2) 2.161(7), Pd(1)–C(4) 1.992(9); P(1)–Pd(1)–N(1) 165.9(2), N(1)–Pd(1)–N(2) 99.4(2), N(1)–Pd(1)–C(4) 80.5(3), P(1)–Pd(1)–N(2) 84.4(2), P(1)–Pd(1)–C(4) 98.0(3), N(2)–Pd(1)–C(4) 170.8(3).



1 *R*-enantiomer



2



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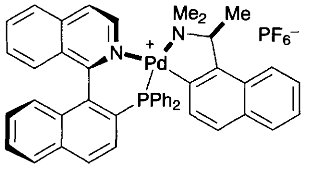

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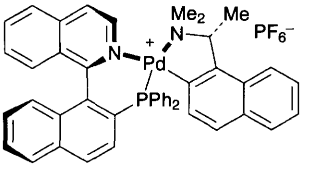

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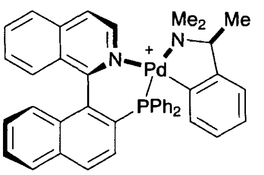
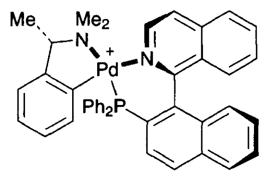
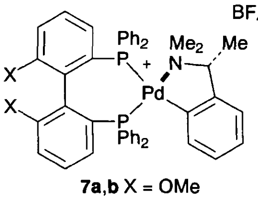


2 PF$_6^-$

6a



6b



7a,**b** X = OMe
8a,**b** X = F

The X-ray structure of complex **6** demonstrates that the Pd cation in the asymmetric unit has the benzylic carbon C(2) disordered 50:50 between positions C(2a) and C(2ba) corresponding to the (*S*,*S*) and (*S*,*R*)-diastereoisomers, shown in Fig. 2 as the (*S*,*S*) form.§ Hence the complex is effectively a quasiracemate.[11] The flapping motion of the five-membered ring exchanges the axial and equatorial methyl groups on N(1), whilst rotating the substituents on C(1) so that C(2) almost moves to the position formerly occupied by H(2) and *vice versa*. The effect of this movement is to attain a conformation of the metallocycle which is very close to being an inversion of the original, although the thermal ellipsoids of C(13) and C(14) [attached to N(1)] are slightly elongated, indicating that some movement of these methyl groups occurs in the alternative structures. The angle between the alternative C(2) positions about C(1) is 74.7°, significantly smaller than the 109° which would correspond to an actual interchange. The result is close enough to a real inversion for the cations of the two complexes (*S*,*R*)-**6a** and (*S*,*S*)-**6b** to pack together as a racemic pair. The relevant fragments shown side-on in Fig. 3 clearly demonstrate this possibility.

With three closely related structures on hand, it is possible to draw some general conclusions. First, the increased conformational rigidity of the naphthylethylamine-derived complexes **4** and **5** leads to their differing stability and easy separation compared to the phenylethylamine analogues. The origin of this rigidity is a strongly unfavourable steric interaction between an equatorial benzylic methyl group and H(8) of the naphthyl residue (Fig. 4) rendering that conformation inaccessible. Detailed inspection of the structures indicates that there are no significant intracomplex H–H or H–C interactions between QUINAP and the metallocycle in either diastereoisomer, but that the metallocyclic ring in the less stable complex **5** is significantly flattened relative to that in the stable isomer **4** which in turn has a very similar conformation to that of complex **6**. Differential strain manifests itself in distortions from square planarity (averting hard interatomic contacts) which are evident from Fig. 5, with the degree of distortion **5** > **4** > **6**. We expect that the increased effective steric bulk associated with complexes derived from **2** compared to those derived from complex **3** will be generally valuable in resolution of bulky ligands.

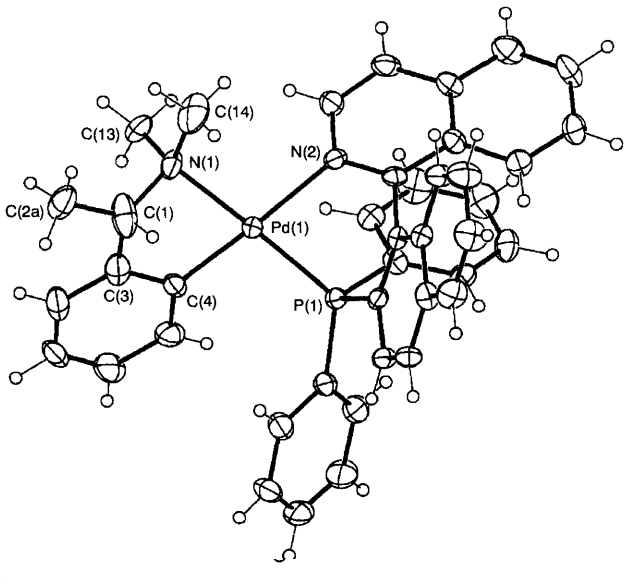


Fig. 2 Molecular structure of complex (**6**) showing one of the two positions for C(2). Selected bond lengths (Å) and angles (°): Pd(1)–P(1) 2.2424(12), Pd(1)–N(1) 2.144(4), Pd(1)–N(2) 2.180(4), Pd(1)–C(4) 1.988(5), N(1)–C(13) 1.485(7), N(1)–C(14) 1.492(7), C(1)–C(2A) 1.485(8), C(1)–C(2B) 1.466(11); P(1)–Pd(1)–N(1) 173.03(12), N(1)–Pd(1)–N(2) 98.7(2), N(1)–Pd(1)–C(4) 80.9(3), P(1)–Pd(1)–N(2) 82.2(1), P(1)–Pd(1)–C(4) 98.8(2), N(2)–Pd(1)–C(4) 175.3(2).

In summary, we have demonstrated that two apparently similar resolving agents, widely utilised in asymmetric ligand synthesis, form Pd complexes which have distinct conformational properties, affecting the ease of separation of derived diastereoisomers. In QUINAP and related examples the effect favours the use of (*R*)-*N*,*N*-dimethyl-1-(1-naphthyl)ethylamine-derived complex **2**, but because of the complexity of factors

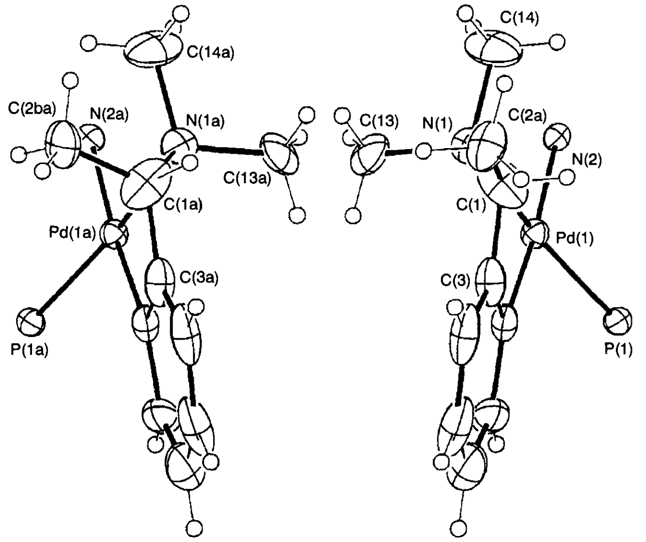


Fig. 3 Edge-on view of the metallocyclic ring in **6** showing the axial *C*-methyl group C(2ba) in the (*S*,*R*)-isomer **6a**, and the equatorial methyl group C(2a) in the (*S*,*S*)-isomer **6b**

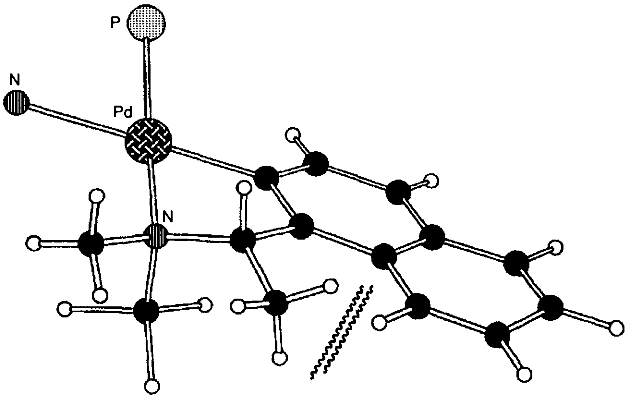


Fig. 4 The 1-naphthyl lock effect showing the steric repulsion arising from the equatorial methyl conformation of the metallocycle (based on the coordinates of structure **6b**

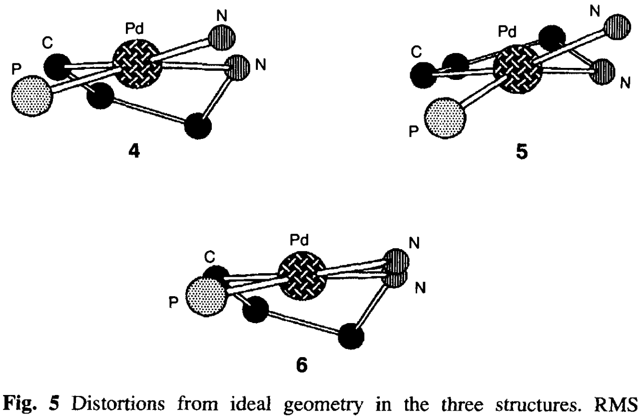


Fig. 5 Distortions from ideal geometry in the three structures. RMS deviations from the square plane for the coordinated atoms are **4** 0.213 Å; **5** 0.400 Å and **6** 0.110 Å.

affecting crystallisation this need not necessarily always be so.[9] As a general guideline, the superiority of complex **2** over complex **3** as a resolving agent for racemic bidentate ligands will be most clearly manifested when they are sterically demanding. In addition, the principle underlying conformational locking in the axial C-methyl form of 1-naphthyl complexes derived from **2** and related compounds may be widely applicable in the design of asymmetric reagents and catalysts.

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Footnotes

† From the (*S*)-enantiomer of **2**

‡ *Crystal data* for **4**: $[C_{45}H_{37}N_2PPd]^+ [PF_6]^- \cdot 2CHCl_3$, $M = 888.1 + 238.7$, orthorhombic, $P2_12_12_1$, $a = 13.232(9)$, $b = 13.983(12)$, $c = 26.011(16)$ Å, $U = 4812$ Å^3, $Z = 4$, $D_c = 1.56$ g cm^{-3}, Mo-Kα radiation, 200 K. Hydrogen atoms were added at calculated positions and refined using a riding model. Anisotropic displacement parameters were used for all non-H atoms; H-atoms were given isotropic displacement parameters of 0.08 Å^3. Weighting scheme $W = 1/\sigma^2(F) + gF^2$. The final R value was 0.054 for 4154 observed reflections.

§ *Crystal data for* **6**: $C_{41}H_{36}F_6N_2P_2Pd$, $M = 839.06$, triclinic, $P\bar{1}$, $a = 11.371(2)$, $b = 12.751(2)$, $c = 15.165(2)$ Å, $\alpha = 97.95(2)°$, $\beta = 110.320(10)°$, $\gamma = 110.010(10)$ deg., $U = 1853.2(5)$ Å^3, $T = 413(2)$ K, $\lambda = 0.71073$ A, $Z = 2$, $D_c = 1.504$ Mg m^{-3}, $F(000) = 852$. μ(Mo-Kα) = 0.650 mm^{-1}. Data collection with the FAST area detector of the SERC Crystallographic service, courtesy of Professor M. B. Hursthouse. The crystal was held at 240(2) K with the Oxford Cryosystem Cryostream Cooler (Cosier & Glazer, 1986). Maximum 2θ was 50°; 8516 reflections measured, 5335 unique [R(int) = 0.0529], no absorption correction. The single cation in the asymmetric unit has C(2) disordered 50 : 50 between the positions corresponding to the *S,R*- and *S,S*-diastereoisomers. Because of the excellent refinement in $P\bar{1}$, no attempt was made to refine using space group $P1$. Hydrogen atoms were added at calculated positions and refined using a riding model. Anisotropic displacement parameters were used for all non-H atoms; H-atoms were given isotropic displacement parameters equal to 1.2 (or 1.5 for methyl hydrogens) times the equivalent isotropic displacement parameter of the atom to which the H-atom is attached. $R1$ [for $> 2\sigma(I)$] = 0.0467, $wR^2 = 0.1297$. Refined parameters 482. Refinement using SHELXL 93 (Sheldrick, 1994). Atomic coordinates, bond lengths and angles, and thermal parameters for both compounds have been deposited at the Cambridge Crystallographic Data Centre. See Information for Authors, Issue No. 1.

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