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An NMR study of the solution conformations of di(tertiary phosphine) complexes of orthopalladated 1-phenyl-1-(*N*,*N*-dimethylamino)ethane

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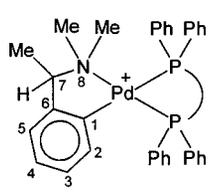
NOE intensities derived primarily from 2-D NMR ROESY spectra were used to study the solution conformations of the chelate rings of the (*R*)- and (*S*)-[1-phenyl-1-(*N*,*N*-dimethylamino)ethane][(2*R*,3*R*)-bis(diphenylphosphino)-butane]palladium(II) cations, **3** and **4**. In each, the diphosphine ring adopts a conformation with both *N*-methyl groups equatorial owing to potential unfavourable trans-annular methyl–phenyl interactions in the alternative conformation with axial methyl groups. For the orthometallated chelate ring the population of the conformer with *C*-methyl equatorial is less than 10% in **4**, but is close to 55% in **3**. This contrasting behaviour is attributed to inter-annular steric interactions between the *N*-methyl and the *P*-phenyl groups which also lead to a weakening of the Pd–N bond in **3** and can account for the enantioselectivity of the orthopalladated 1-phenyl-1-(*N*,*N*-dimethylamino)ethane moiety when used as a resolving agent.

Introduction

Chiral orthometallated palladium complexes of 1-phenyl-1-(*N*,*N*-dimethylamino)ethane and 1-(1-naphthyl)-1-(*N*,*N*-dimethylamino)ethane are extensively used for the resolution of racemic mixtures,[1] the assignment of the absolute configuration [2] and regio-isomerism of optically active ligands,[3] and the investigation of diastereoselectivity in synthetic processes [4] by the formation of adducts such as **1** and **2**.



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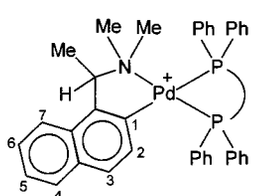

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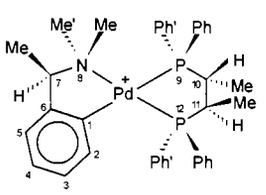
It has generally been found that the naphthyl adducts **2** provide greater enantiomeric discrimination than their phenyl counterparts **1**, sometimes to the extent that resolution can succeed with the former and fail with the latter. It has been proposed that this is due to the ability of **1** to adopt a conformation of the puckered five-membered orthometallated chelate ring in which the *C*-methyl group is either axial [conformer *a*] or equatorial [conformer *e*], whereas **2** is restricted to the former situation.[5] [The λ/δ description is not used in this paper because it leads to an apparent change in conformation of *R* and *S* enantiomers.] This interpretation is supported by X-ray diffraction studies which show that in no case is the *e*-conformation of the orthometallated chelate ring found for **2** whereas either conformer can occur for **1**.[1c,1f–i,5,6] In the case of **2**, molecular models confirm that the *e*-conformation will be of very high energy owing to steric interaction between the *C*-methyl group and H7 of the naphthyl group;[5] this leads to conformational locking and thus the solid state results probably also apply in solution. However, this is not so for **1** and it is therefore of interest to determine the solution conformations of complexes of this type.

In this paper we report detailed NMR studies of the solution conformations and inter-annular interactions of each chelate ring of the two diastereomers of the [1-phenyl-1-(*N*,*N*-dimethylamino)ethane][(2*R*,3*R*)-bis(diphenylphosphino)butane]-palladium(II) cations **3** and **4** using proton NOE measurements augmented by information from coupling constants.



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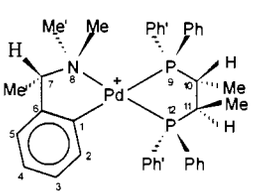

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Previously, we have used this approach in a more qualitative way to confirm the absolute configuration of the di(tertiary phosphine) (*R*,*R*)-CHIRAPHOS [(2*R*,3*R*)-bis(diphenylphosphino)butane].[2a] This work also showed a striking difference in δ(H7) and δ(^{13}CMe7) for **3** and **4** which is probably related to differences in conformer populations of the orthometallated chelate ring. The data presented here are primarily derived from 2-D rotating frame nuclear Overhauser effect (ROESY)[7] experiments as these are effectively independent of molecular tumbling rate. By contrast, laboratory frame NOE measurements (including NOESY spectra) are sensitive to the relationship between the molecular tumbling rate and the measuring frequency and for our species this may lead to NOE enhancements of either sign or even zero.

Experimental

Diastereomerically pure **3** and **4** were prepared as their hexafluorophosphate salts as follows: (2*R*,3*R*)-bis(diphenylphosphine)butane (Aldrich) (42.6 mg, 0.1 mmol) and (*R*,*R*)- or (*S*,*S*)-bis[1-phenyl-1-(*N*,*N*-dimethylamino)ethane-μ-chloropalladium] (27.5 mg, 0.05 mmol) were shaken with methanol (5 cm^3) until a clear pale yellow solution was obtained (15 min). To this was added a solution of ammonium hexafluorophos-

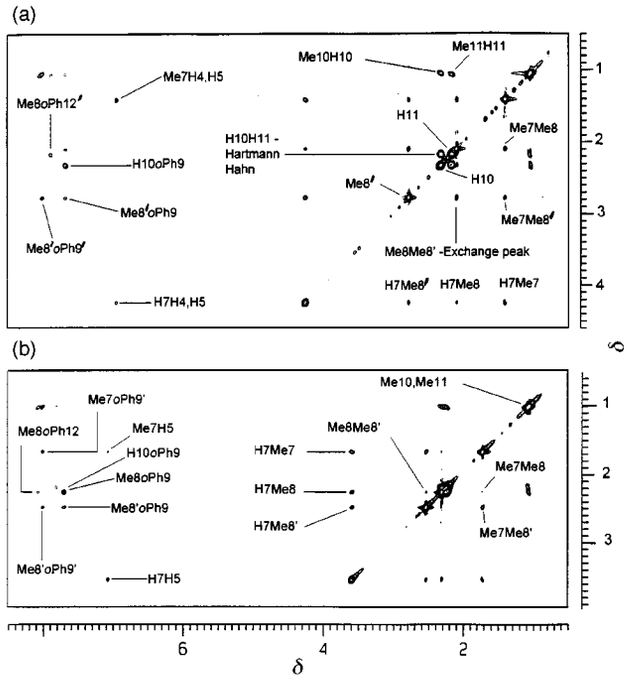


Fig. 1 Portions of 500 MHz proton ROESY spectra of (a) **3** and (b) **4** in $CDCl_3$ at 295 K with spin-locking (mixing) times of 130 ms.

phate (25 mg, 0.15 mmol) in methanol (5 cm^3); precipitation began within a few minutes and after storage at −20 °C for 1 h the product was filtered off as fine white crystals which were washed three times with cold methanol and then dried. The yield was 69 mg, 85%. Samples were examined as de-aerated *ca.* 0.03 M solutions in $CDCl_3$ and these solutions retained their diastereomeric purity when stored for several months at room temperature.

^1H, ^{13}C and ^{31}P NMR spectra were obtained at 500.14, 125.75 and 202.2 MHz respectively on a Bruker AMX 500 spectrometer using 5 mm outer diameter tubes which were spun for 1-D experiments and stationary for 2-D ones. Phase sensitive 2-D proton ROESY[7] spectra were obtained using the pulse sequence 90°–t_1–spin lock–acquire(t_2) with phase cycling by the time-proportional phase incrementation (TPPI) method. Typically, 32 transients were acquired into 1 K data points for each of 512 values of t_1 and a sine-bell weighting function was used in each dimension prior to Fourier transformation into a 1 K × 1 K data matrix. The spectral width in each dimension was 4500 Hz and the transmitter was set at the centre of the range. The spin-locking field had $\gamma B_1/2\pi = 5000$ Hz, the spin-locking (mixing) times ranged from 50–300 ms, and a recycling delay of 1 s was used. The spectra are presented with positive main diagonal peaks, *i.e.* negative ROESY peaks. For the selective inversion experiments[8] the pulse sequence $180°_{sel}$–τ–90° was used and the data were acquired in the difference mode using a relaxation delay of 3 s and a pulse length of 30 ms for the selective 180° pulse with τ values incremented between 0 and 1.6 s. Spin lattice relaxation times were measured using the standard inversion–recovery method.

Results

(A) Assignments

Table 1 gives proton and ^{13}C chemical shifts for **3** and **4**. The assignment strategy depended upon selective ^1H-{^{31}P}, DQF-COSY,[9] ROESY[7] (Fig. 1) and HMQC[10] experiments. The ^{31}P-{^1H} spectrum is a pair of doublets at δ 63.4 and 43.9, $^2J(^{31}P–^{31}P) = 39.3$ Hz in **3**, and δ 62.7 and 44.4, $^2J(^{31}P–^{31}P) = 39.9$ Hz in **4**, the chemical shift separations being large enough for selective ^1H-{^{31}P} decoupling experiments to be feasible as illustrated in Fig. 2.

Table 1 ^1H and ^{13}C NMR data for **3** and **4** in $CDCl_3$[a]

	$\delta(^1H)$		$\delta(^{13}C)$	
Position	**3**	**4**	**3**	**4**
2[b]	6.64	6.69	136.5	136.8
3[c]	6.58	6.62	126.1	125.8
4[d]	6.90	6.90	125.7	125.8
5	6.93	7.06	123.7	122.6
7[e]	4.24	3.56	75.0	78.4
Me7	1.37	1.70	16.4	26.1
Me8	2.07	2.28	45.4	51.2
Me8′	2.76	2.51	51.6	49.8
o-Ph9	7.65	7.70	133.8	131.8
o-Ph9′	7.98	8.00	134.6	136.5
m-Ph9	7.65[j]	7.70[c]	130.2	130.1
m-Ph9′	7.77	7.71	129.9	129.8
10[f]	2.29	2.28	38.3	37.9
Me10[g]	1.02	1.03	13.8	13.4
11	2.15	2.22	40.5	39.6
Me11[h]	1.05	1.05	15.0	14.9
o-Ph12	8.01	8.07	136.0	136.4
o-Ph12′	7.85	7.80	133.1	132.4
m-Ph12	7.70	7.75	128.9	129.6
m-Ph12′	7.59	7.50	129.6	129.5
p-Ph[i]	7.77	7.81	133.5	133.5
	7.71	7.81	132.1	133.6
	7.58	7.51	132.1	131.9
	7.67	7.65	131.7	131.7

[a] Proton and ^{13}C chemical shifts are in ppm ± 0.01 ppm relative to $SiMe_4$; $^{31}P–^{13}C$ couplings in the phenyl groups are: $^3J(^{31}P–^{13}C_{ortho})$ 10.2–14.0, $^4J(^{31}P–^{13}C_{meta})$ 9.5–11.4, $^5J(^{31}P–^{13}C_{para}) \approx 2$ Hz; others are in Table 2. [b] $^3J(H_2–H_3) = 7.3 \pm 0.1$ Hz in **3** and **4**; $^4J(H_2–H_4) = 1.0 \pm 0.1$ Hz in **3** and **4**. [c] $^3J(H_3–H_4) = 7.3 \pm 0.1$ Hz in **3** and **4**; $^4J(H_3–H_5) = 1.8 \pm 0.1$ Hz in **3** and **4**. [d] $^3J(H_4–H_5) = 7.5 \pm 0.1$ Hz in **3** and **4**. [e] $^3J(H_7–Me_8) = 6.6 \pm 0.1$ Hz in **3** and **4**. [f] $^3J(H_{10}–H_{11}) = 13.6 \pm 0.1$ Hz in **3**; 13.7 ± 0.1 Hz in **4**. [g] $^3J(H_{10}–Me_{10}) = 6.8 \pm 0.1$ Hz in **3**; 6.6 ± 0.1 Hz in **4**. [h] $^3J(H_{11}–Me_{11}) = 6.7 \pm 0.1$ Hz in **3**; 6.6 ± 0.1 Hz in **4**. [i] Resonances not assigned to individual phenyl rings but ^{13}C and ^1H are correlated as shown. [j] Overlapped signal, position (± 0.03 ppm) obtained from H/C correlation spectrum.

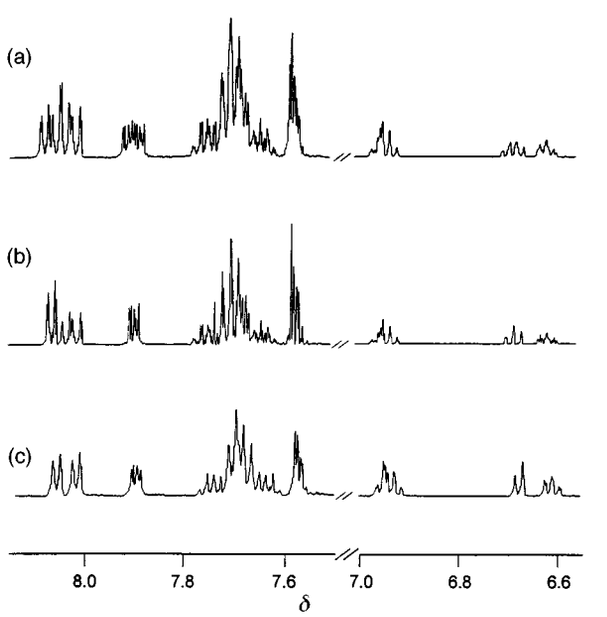
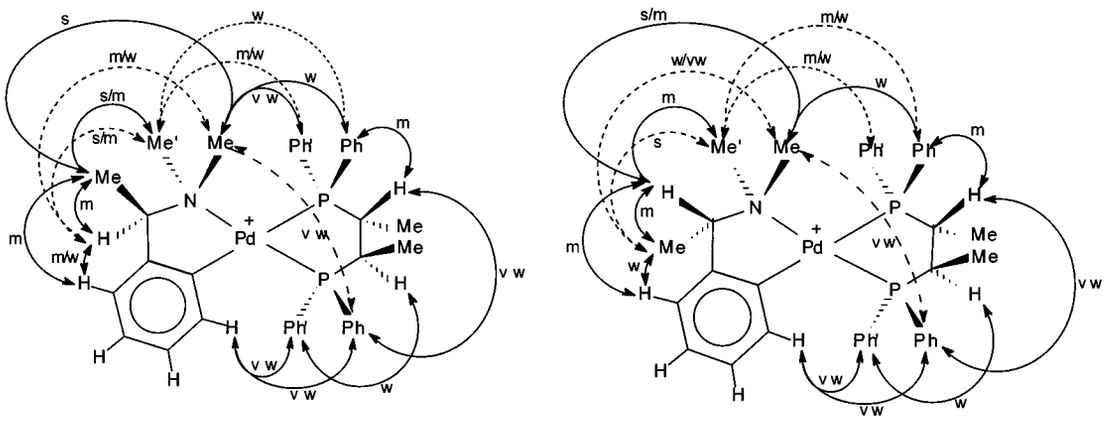


Fig. 2 High-frequency parts of 500 MHz proton spectra of **3** in $CDCl_3$ at 295 K. (a) Normal spectrum. (b) With P12 decoupled. (c) With P9 and P12 decoupled.

(B) Stereochemistry

The absolute configuration of **3** was derived by using the NOE interactions in the ROESY spectrum to relate the configuration at C10 and C11 to the known (*R*) configuration at C7. Fig. 3 summarizes these interactions and shows for example how (i)



3 **4**

Fig. 3 Patterns of NOE interactions in **3** and **4** derived from volume integrals of off-diagonal peaks in proton ROESY spectra at 500 MHz with a mixing time of 130 ms, s = strong, m = medium, w = weak, vw = very weak.

Me7 is sterically related to Me8 and Me8′, (ii) Me8 and Me8′ are sterically related to *ortho*-Ph9 and *ortho*-Ph9′, and (iii) *ortho*-Ph9 and *ortho*-Ph9′ are sterically related to Me10 and H10, thus showing the configuration at C10 to be *R*. It then follows that C11 is also *R*. The *ortho*-Ph12 and *ortho*-Ph12′ protons are sterically assigned by a long range trans-annular interaction between Me8 and *ortho*-Ph12 indicating that these sites are on the same "side" of the coordination "plane". The designations of the NOE peaks as strong (s), medium (m) *etc*. were derived from volume integrals. In a similar way the configurations at C10 and C11 in **4** were shown to be *R* relative to the *S* configuration at C7 [Figs. 1(b) and 3(right)].

(C) Chemical exchange effects

In ROESY spectra off-diagonal peaks arising from direct NOE interactions are negative (on the convention that the diagonal peaks are positive)[11] whereas those from chemical exchange or Hartmann–Hahn interactions are positive. The ROESY spectrum of **3** [Fig. 1(a)] has strong positive off-diagonal peaks between Me8 and Me8′ which cannot arise from a Hartmann–Hahn interaction since these protons are not scalar coupled; nor can they be due to an indirect NOE owing to their large magnitude. They must therefore result from a relatively slow chemical exchange process and this was followed in more detail by a selective inversion magnetization transfer experiment. In the absence of cross-relaxation between the exchanging methyls themselves and with other sites, and provided that T_1(Me8) = T_1(Me8′), then the exchange rate can be obtained by plotting ln $\{(I_\infty + S_\infty) - (I_\tau + S_\tau)]/I_\infty\}$ and ln $\{I_\tau - S_\tau)/I_\infty\}$ against the delay time τ where I and S refer to the intensities of the inverted and exchanging methyls respectively.[12] In our system all NOEs involving Me8 and Me8′ are much weaker than the exchange peaks, and T_1(Me8) = 0.24 s and T_1(Me8′) = 0.26 s so that the foregoing assumptions are justified. This method yielded a rate constant for the exchange process of 0.16 ± 0.03 s^{-1} at 295 K corresponding to a $\Delta G^\ddagger$ of 100.5 kJ mol^{-1}. Behaviour of this kind was not observed for **4**.

(D) Conformations

(i) The diphosphine ring. Fig. 4 shows Newman projections down the C10–C11 bond for the two conformations of the five-membered puckered (*R*,*R*)-CHIRAPHOS ring. In principle, the populations of these two forms can be determined from NOE interactions such as Me10/Me11 and H10/H11, but in practice scalar coupling interactions make this difficult from ROESY data.[11]

Table 2 Couplings[a] to ^{31}P in **3** and **4**

	$J(^{31}P_9–H)$		$J(^{31}P_{12}–H)$		$J(^{31}P–^{31}C)$	
Position	**3**	**4**	**3**	**4**	**3**	**4**
2	7.7	7.8	5.6	5.2	*b*	10.2, 3.2
3	2.5	1.9	0.6	0.7	8.3, 5.1	8.4, 5.7
5	2.2	2.9	—	—	7.1	5.7
7	—	—	2.6	6.3	—	—
Me8	1.2	0	2.8	1.7	—	—
Me8′	2.0	3.3	2.8	3.9	—	—
10	4.0	3.5	8.2	7.0	26.3, 12.9	28.0, 14.0
Me10	11.1	11.2	—	—	15.3, 5.7	16.5, 6.4
11	8.1	7.0	6.5	6.7	31.8, 22.9	33.1, 21.3
Me11	—	—	12.3	13.5	17.8, 5.1	19.1, 5.7

[a] Coupling constants are in Hz, ±0.1 Hz. [b] Details of multiplicity hidden by overlap.

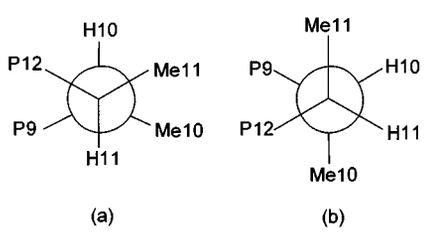


Fig. 4 Newman projections down C11–C10 for idealized conformations of the (*R*,*R*)-CHIRAPHOS chelate ring. (a) Equatorial methyl groups. (b) Axial methyl groups.

Fortunately, it was possible to use the ^3J(H–H) and $^3J(^{31}P–H)$ couplings obtained from spectral simulations[13] (Fig. 5) in conjunction with the Karplus equation[14] to determine the conformations. From Table 2 it can be seen that in **3** and **4** respectively (i) ^3J(P9–H11) = 8.1 and 7.0 Hz and (ii) ^3J(P12–H10) = 8.2 and 7.0 Hz. Together with ^3J(H–H) = 13.6 and 13.7 Hz, this is consistent with H10 and H11 being axial in both **3** and **4** and hence with equatorial methyl groups in each isomer.

(ii) The orthometallated chelate ring. Each of the two conformations of the orthometallated chelate ring in **3** has two H/*N*-Me and two *C*-Me/*N*-Me NOE interactions giving a total of eight potentially different interactions, together with a further eight in **4**. However, provided that these five-membered rings have essentially identical bond lengths and interbond angles, and in particular that the dihedral angles α about the C7–N8 bond are the same, this number reduces to the three different

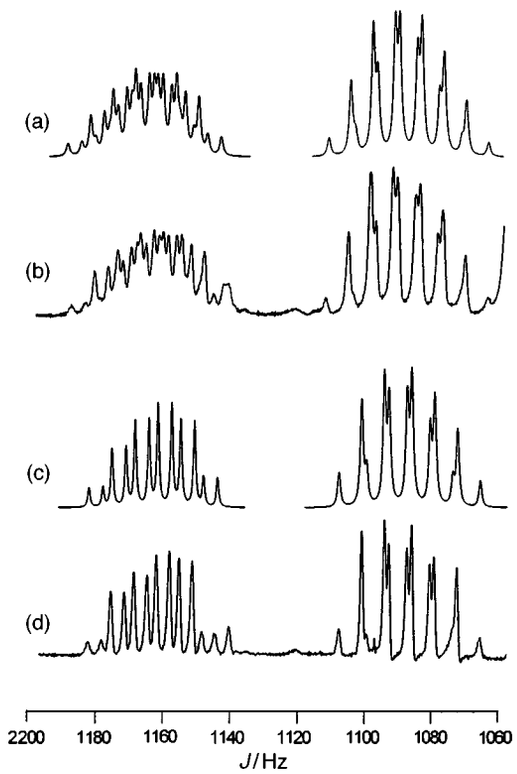


Fig. 5 H10 (left) and H11 (right) regions of the 500 MHz proton spectrum of **3**. (a) Simulated spectrum using parameters of Table 2. (b) Experimental spectrum. (c) Simulated spectrum without couplings to P12. (d) Experimental spectrum with P12 decoupled.

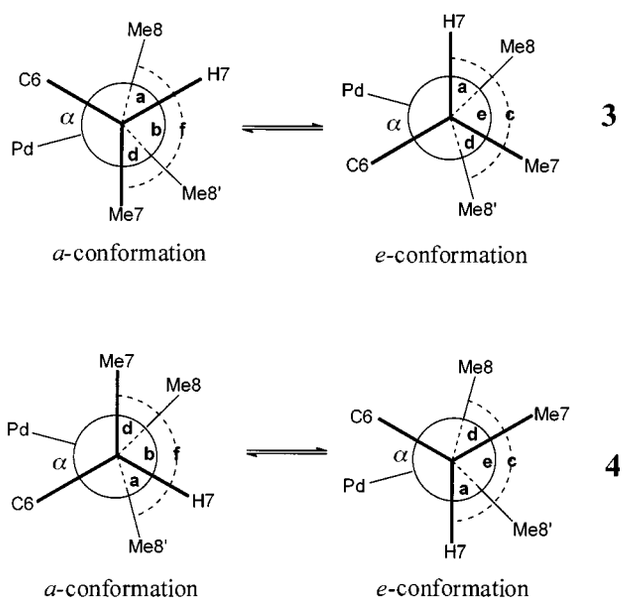


Fig. 6 Newman projections down the C7–N8 bond for different conformations of the orthometallated ring in **3** and **4** showing sets **a** to **f** of equal NOE interactions.

H7/*N*-Me interactions **a**, **b** and **c** and the three different Me7/*N*-Me interactions **d**, **e**, and **f** designated in Fig. 6. X-Ray data available for other derivatives containing the orthopalladated 1-phenyl-1-(*N*,*N*-dimethylamino)ethane unit show α to range from 41 to 44° thus supporting this assumption.[15] It is then possible to use the observed relative NOE intensities involving H7, Me7, Me8 and Me8′ to deduce the populations of the *a*- and *e*-conformations of the orthometallated chelate rings in **3** and **4** under the following restrictions. (a) The extreme narrowing condition applies (note that this implies that data from NOESY experiments should also be suitable for this study), spin lattice relaxation is dominated by efficient intra-methyl dipole–dipole relaxation,[16] cross relaxation back to the diagonal component is negligible, and the methyl group internal motions are essentially identical. (b) The rates of interchange of the two conformers of the orthometallated chelate rings of **3** and of **4** are fast on the ^{1}H NMR chemical shift timescale, but slow compared to the molecular tumbling rate as is apparent from the observation of averaged spectra from the two conformations at all accessible temperatures at 500.14 MHz. It is then permissible to average the NOE intensities rather than the relaxation rates themselves according to the populations of each conformer.[17] (c) Exchange of Me8 and Me8′ in **3** is slow compared with the rate of interchange of the conformers. This follows from (b) above and the observation of separate Me8 and Me8′ signals. Note that potential TOCSY artefacts are not important here since there is no scalar coupling between the relevant protons.

Then for **3** the ratio, H_R, of the observed H7/Me8 and H7/Me8′ NOE intensities will be given by eqn. (1) and the ratio,

$$H_R = [r\mathbf{a} + (1 - r)\mathbf{a}]/[r\mathbf{b} + (1 - r)\mathbf{c}] = \mathbf{a}/[r\mathbf{b} + (1 - r)\mathbf{c}] \quad (1)$$

M_R, of the observed Me7/Me8 and Me7/Me8′ NOE intensities will be given by eqn. (2), where r is the mole fraction of the

$$M_R = [r\mathbf{f} + (1 - r)\mathbf{e}]/[r\mathbf{d} + (1 - r)\mathbf{d}] = [r\mathbf{f} + (1 - r)\mathbf{e}]/\mathbf{d} \quad (2)$$

a-conformation in **3** and **a** to **f** are the intensities of the corresponding NOE interactions. Similarly, for **4** the corresponding ratios H_S and M_S are given by eqns. (3) and (4), where s is the mole fraction of the *a*-conformation in **4**.

$$H_S = [s\mathbf{b} + (1 - s)\mathbf{c}]/[s\mathbf{a} + (1 - s)\mathbf{a}] = [s\mathbf{b} + (1 - s)\mathbf{c}]/\mathbf{a} \quad (3)$$

$$M_S = [s\mathbf{d} + (1 - s)\mathbf{d}]/[s\mathbf{f} + (1 - s)\mathbf{e}] = \mathbf{d}/[s\mathbf{f} + (1 - s)\mathbf{e}] \quad (4)$$

Hence from eqns. (1) and (3) and from eqns. (2) and (4) we obtain eqns. (5) and (6) respectively.

$$H_R H_S = [s\mathbf{b} + (1 - s)\mathbf{c}]/[r\mathbf{b} + (1 - r)\mathbf{c}] \quad (5)$$

$$M_R M_S = [r\mathbf{f} + (1 - r)\mathbf{e}]/[s\mathbf{f} + (1 - s)\mathbf{e}] \quad (6)$$

If the NOE interactions between groups that are *anti* are much weaker than between those that are *gauche*, *i.e.* if $\mathbf{c} \ll \mathbf{b}$ and $\mathbf{f} \ll \mathbf{e}$ then eqns. (5) and (6) reduce to $H_R H_S = s/r$ and $M_R M_S = (1 - r)/(1 - s)$ whence r and s can be calculated from the experimentally determined ratios H_R, H_S, M_R, and M_S. Using the intensities of the off-diagonal peaks in the ROESY spectra with mixing times of 130 ms this method gave values for the mole fractions of the *a* conformer of the orthometallated chelate ring in **3** and **4** of 45 and >90% respectively. It is important to appreciate that this result is not dependent upon any direct comparison of the intensities of H-to-methyl with methyl-to-methyl NOE interactions.

The approximation *anti* $\ll$ *gauche* with respect to the Me7/Me8(Me8′) NOEs is probably very realistic, but this is not necessarily so for the H7/Me8(Me8′) interactions. However, the expected ratio **b**/**c** of the *gauche* and *anti* H7/Me8 NOE interactions can be calculated by using interatomic distances from the orthometallated chelate ring in the analogous [(*R*)-1-phenyl-1-(*N*,*N*-dimethylamino)ethane][bis(diphenylphosphino)-ethane]palladium(II) cation for which a solid state geometry is available.[15] Different results are obtained according to the assumptions made regarding the averaging of the rotation of the methyl groups.[17,18] When the methyl group rotation is slow compared with molecular tumbling it is appropriate to use $\langle r^{-6} \rangle$ averaging over all dihedral angles and the **b**/**c** ratio is then calculated to be 4.0:1. When the methyl group rotation is fast compared with molecular tumbling $\langle r^{-3} \rangle^2$ averaging

should be used and this gives a ratio of 3.4:1. The ratios calculated for a three site jump model with a staggered methyl conformation are 4.7:1 and 4.0:1 for $\langle r^{-6} \rangle$ and $\langle r^{-3} \rangle^2$ averaging respectively.

Similarly, using the same X-ray structural data, the Me7/Me8 *gauche*/*anti* ratio **e**/**f** can be calculated as 15:1 for $\langle r^{-6} \rangle$ averaging and 8:1 for $\langle r^{-3} \rangle^2$ averaging over three sites in each case. It thus follows that in all cases the initial *anti* ≪ *gauche* approximation is in fact a reasonable one, and that the conclusions regarding the relative populations of the *a*- and *e*-conformers are valid.

Discussion

The effectiveness of the orthometallated palladium moieties as resolving agents must depend upon some form of interaction between the chiral carbon of the amine ring and the chiral centre(s) of the tertiary phosphine, diphosphine or other chiral ligand. These centres are typically 5 Å or more apart and direct steric interaction is therefore unlikely; rather there must be a series of interactions involving the intermediacy of the *P*-phenyl and *N*-methyl groups.

Irrespective of the NOE averaging model used to determine the conformational ensemble of the orthometallated chelate ring it is clear that there is a marked difference between **3** and **4** with axial *C*-methyl conformer populations of *ca.* 45% and >90% respectively. This observed population difference can be rationalized in terms of competition between the inter-annular non-bonded P9-phenyl/*N*-methyl group interactions and the preferred low energy conformations of the orthometallated and diphosphine chelates.

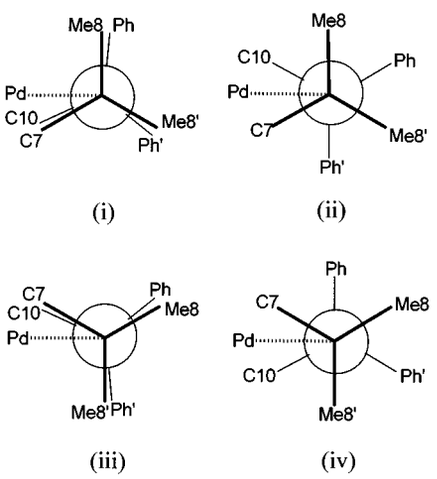


Fig. 7 Newman projections down the N8–P9 vector for different conformations of the (*R*,*R*)-CHIRAPHOS and orthometallated chelate rings in **3** and **4**. (i) Me10, Me11 equatorial; Me7 axial in **3**, equatorial in **4**. (ii) Me10, Me11 axial; Me7 axial in **3**, equatorial in **4**. (iii) Me10, Me11 equatorial; Me7 equatorial in **3**, axial in **4**. (iv) Me10, Me11 axial; Me7 equatorial in **3**, axial in **4**.

In the present study, the (*R*,*R*)-CHIRAPHOS ring has been shown to adopt exclusively the conformation with equatorial methyl groups (Fig. 4) in both **3** and **4**, presumably because this minimizes trans-annular di-axial interactions between the *C10*- and *C11*-methyl and the *P*-phenyl groups.[19] The P9-phenyl/*N*-methyl interactions can be visualized by means of the Newman projections down the N–P9 vector as shown in Fig. 7. Of these, conformations 7(ii) and 7(iii) are excluded because they would require the CHIRAPHOS chelate ring to have axial methyl groups and thus the pattern of available overall conformations is as shown in Fig. 8. In **3** 8(i) is destabilized relative to 8(ii) by the eclipsed *N*-methyl/*P*-phenyl inter-annular interactions, but 8(ii) is destabilised relative to 8(i) by the having *C*-methyl equatorial which leads to unfavourable steric interactions with benzyl H5 and *two* rather than one *N*-methyl groups. Hence overall 8(i) and 8(ii) are of comparable energy leading to comparable populations. By contrast, in **4** 8(iii) experiences none of these destabilising interactions whereas 8(iv) has all three and thus will be significantly less stable than 8(iii) leading to an *a* population in excess of 90%. Although the derivation of the conformer populations in the Results section makes use of several approximations, overall it is clear that experimentally in **3** the *a*/*e* ratio is ≈1:1 whereas in **4** it exceeds 9:1, in accord with the foregoing discussion.

It is striking that while for **3** each accessible conformation of the orthometallated chelate ring is subject to at least one destabilizing interaction, for **4** the *a*-conformation is not and is therefore of significantly lower energy than either conformer in **3**. This difference in the overall relative stabilities of **3** and **4** is vividly exemplified by the weakening of the N–Pd bond in the former. This occurs to the extent that in **3** reversible bond cleavage can occur followed by inversion at the nitrogen thus accounting for the observed slow exchange of Me8 and Me8′ with a free energy of activation of 100.5 kJ mol^{-1} at 295 K, a process which does not occur measurably in **4**.

Certain of the other NMR parameters of **3** and **4** also reflect different conformer populations of these species. Most notably, δ H7 is 0.71 ppm higher in **3** than in **4** and this is the direction

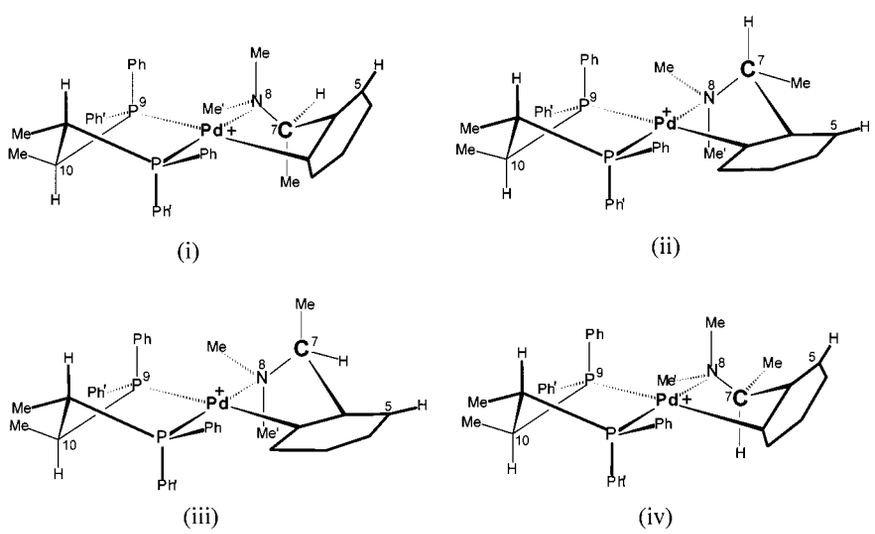


Fig. 8 Overall conformations of **3** and **4** with the (*R*,*R*)-CHIRAPHOS ring in the conformation having equatorial methyl groups. (i) **3** with orthometallated chelate ring in *a*-conformation. Population 45%. (ii) **3** with orthometallated chelate ring in *e*-conformation. Population 55%. (iii) **4** with orthometallated chelate ring in *a*-conformation. Population >90%. (iv) **4** with orthometallated chelate ring in *e*-conformation. Population <10%.

to be expected from the influence of the ring current on protons in or near the plane of the orthometallated chelate ring. The ^{13}C Me7 shifts are significantly more affected (δ 16.4 for **3** and 26.1 for **4**); this is too large a difference to be due to a ring current and probably results from a Me–Me γ effect.[20] This induces shielding and hence the ^{13}C Me7 should resonate at a higher field in **3** than in **4** since in the *e*-conformer (55% population in **3**) there are two Me–Me *gauche* γ interactions. In contrast the *a*-conformation in **4** is over 90% populated and has only one Me–Me *gauche* interaction. The significant difference between the values of ^{4}J(P12–H7) in **3** and **4** can also be attributed to a different distribution of conformers and it seems likely that these parameters may be potentially diagnostic of the conformational preferences in these species.

We have thus demonstrated that different patterns of intra- and inter-annular interactions lead to markedly different conformational ensembles in the diastereomers **3** and **4**. This is not withstanding a spatial separation of the relevant chiral centres in excess of 5 Å and is reflected in different overall stabilities as exemplified by the strength of the N–Pd bond in the two species. We believe that these differences may also contribute to the effectiveness of 1-phenyl-1-(*N*,*N*-dimethylamino)ethane- and 1-(1-naphthyl)-1-(*N*,*N*-dimethylamino)ethane-palladium complexes as resolving agents for phosphines and diphosphines. Normally, this ability would be ascribed primarily to variations in lattice forces in the solid; however, it is clear from several X-ray structures[13] in which the unit cell contains molecules of each conformation that such variations may well be minimal. Hence it may be that the resolving capabilities of these complexes are determined primarily by differences in intramolecular stability which persist in solution, and this opens up the prospect of the rational design of resolving agents for particular enantiomeric pairs. It has also been found[2b,21] that the orthometallated [1-(1-naphthyl)-1-(*N*,*N*-dimethylamino)-ethane]palladium species can function as a remarkably effective chiral auxiliary in asymmetric synthesis, and it again seems likely that this is due to similar sequences of non-bonded intra-molecular interactions.

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