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Synthesis of bis[palladium(II)] and bis[platinum(II)] complexes containing chiral, linear quadridentate ligands with a P_2N_2 donor set †

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Received 30th July 2001, Accepted 29th October 2001
First published as an Advance Article on the web 10th December 2001

A number of bis[palladium(II)] and bis[platinum(II)] complexes of the type [$(MCl_2)_2$(μ-quadridentate)] [where M = Pd(II) or Pt(II)] and [$(PtClMe)_2$(μ-quadridentate)] have been prepared containing the linear quadridentate NPPN ligands 1,3-bis[(2-aminophenyl)phenylphosphino]propane, **1**; 1,4-bis[(2-aminophenyl)phenylphosphino]butane, **2**; 1,5-bis[(2-aminophenyl)phenylphosphino]pentane, **3** [Pd(II) only]; 1,6-bis[(2-aminophenyl)phenylphosphino]hexane, **4**; and 1,3-bis[(2-aminoethyl)phenylphosphino]propane, **5**; and the related PNNP ligands 1,3-bis[(2-diphenylphosphinophenyl)amino]propane, **6**; and 1,2-bis[(2-diphenylphosphinophenyl)amino]ethane, **7** [Pt(II) only]. Separation of the racemic and meso diastereomers of the linear quadridentate NPPN ligands and the resolution of (R_P*,R_P*)-**1** have been achieved *via* separation by fractional crystallisation of a pair of bis[palladium(II)] complexes containing the respective ligand and orthometallated *N*,*N*-dimethylbenzylamine or (*S*)-dimethyl(1-phenylethyl)amine, respectively. The structure of the bis[palladium(II)] complex containing (R_P,R_P)-**1** has been confirmed by X-ray analysis and shown to have the configuration (S_P,S_P,*S*,*S*). Subsequent reaction of stereoisomerically pure [{Pd(2-$C_6H_4CH_2$-NMe_2)}$_2$(μ-L)]$(PF_6)_2$ with HCl gave the corresponding complexes [$(PdCl_2)_2$(μ-L)] [where L = (R_P*,R_P*)-**1**–**5**, (R_P,R_P)- or (S_P,S_P)-**1**, (R_P*,S_P*)-**1**, **-2** or **-5**]. The analogous complex [$(PdCl_2)_2$(μ-**6**)] has been prepared in a similar manner. Bis[platinum(II)] complexes of the type [$(PtClMe)_2$(μ-L)] [where L = (R_P*,R_P*)-**1**, **-2** or **-4**; (R_P,R_P)-, (S_P,S_P)- or (R_P*,S_P*)-**1**; **6** or **7**] have been prepared by reaction of L with [PtCl(Me)(cod)] (cod = cyclocta-1,5-diene). Further treatment with HCl gave the analogous complexes [$(PtCl_2)_2$(μ-L)] [where L = (R_P*,R_P*)-**1**, **-2**, **-4** or **-5**; (R_P*,S_P*)-**1** or **-5**; or **6**]. The dinuclear compounds and, in particular, the bis[platinum(II)] complexes, are seen as potential anticancer agents. Preliminary *in vitro* biological studies have shown them to be active against the murine P388 leukaemia cell-line with cytotoxicities of certain of these complexes being comparable to that of cisplatin.

Several linear quadridentate P_2N_2 ligands containing stereogenic phosphorus donor atoms and terminal primary amine groups have been reported in the literature.[1–4] The ligands typically contain 2–4 methylene linkages between the phosphorus centres and a 1,2-phenylene or 2–3 methylene units linking the phosphorus and nitrogen atoms. Quadridentate ligands of this type exist in racemic and meso diastereomeric forms, however, only in the case of 1,3-bis(2-aminophenyl)-phenylphosphino]propane, **1**, has their separation been reported, by complexation to platinum(II).[4] Two mononuclear cations [PtCl{(R_P*,R_P*)-**1**}]$^+$ and [Pt{(R_P*,S_P*)-**1**}]$^{2+}$ were identified in which the two diastereomeric forms of the ligand were coordinated in a tridentate and tetradentate fashion, respectively. The structure of the former was confirmed by X-ray analysis and clearly established that only one of the terminal primary amine groups of (R_P*,R_P*)-**1** was coordinated to the metal centre. A similar mode of coordination was observed in the dinuclear rhodium(I) complex [{Rh(CO)}$_2$(μ-{(R_P*,R_P*)-**1**})$_2$].[4] Here a mono-deprotonated PN bidentate group from one quadridentate ligand and a phosphorus atom from the other were coordinated to the same metal centre.

In this paper we report on an alternative method of separation of (R_P*,R_P*)- and (R_P*,S_P*)-**1** and the resolution of the former, in both cases by the fractional crystallisation of bis[palladium(II)] complexes containing the ligand and orthometallated *N*,*N*-dimethylbenzylamine or (*S*)-dimethyl(1-phenylethyl)amine, respectively. The separation of the (R_P*,R_P*) and (R_P*,S_P*) forms of several related linear quadridentate P_2N_2 ligands, *viz*. 1,4-bis[(2-aminophenyl)phenylphosphino]butane, **2**, 1,5-bis(2-aminophenyl)phenylphosphino]-pentane, **3**, 1,6-bis(2-aminophenyl)phenylphosphino]hexane, **4**, and 1,3-bis[(2-aminoethyl)phenylphosphino]propane, **5**,[1] using a similar methodology is also described. Subsequent reaction of the complexes with HCl provides a route to the related bis-[dichloropalladium(II)] compounds [$(PdCl_2)_2$(μ-quadridentate)]. The preparation of the analogous bis[dichloropalladium(II)] complex containing 1,3-bis[(2-diphenylphosphinophenyl)-amino]propane, **6**,[5] is also described. Several examples of dinuclear palladium(II) complexes containing linear quadridentate P_2N_2 ligands with terminal diphenylphosphino or oxazolyl groups have been reported in the literature.[6]

A preparative route to the analogous bis[dichloroplatinum-(II)] complexes [$(PtCl_2)_2$(μ-quadridentate)] is also described *via* the reaction of appropriate forms of the quadridentate ligands with (1,5-cyclooctadiene)chloromethylplatinum(II), to give [$(PtClMe)_2$(μ-quadridentate)], followed by treatment with HCl. The synthesis of the related complexes [$(PtClMe)_2$(μ-L)] [where

† Electronic supplementary information (ESI) available: experimental details. See http://www.rsc.org/suppdata/dt/b1/b106861j/

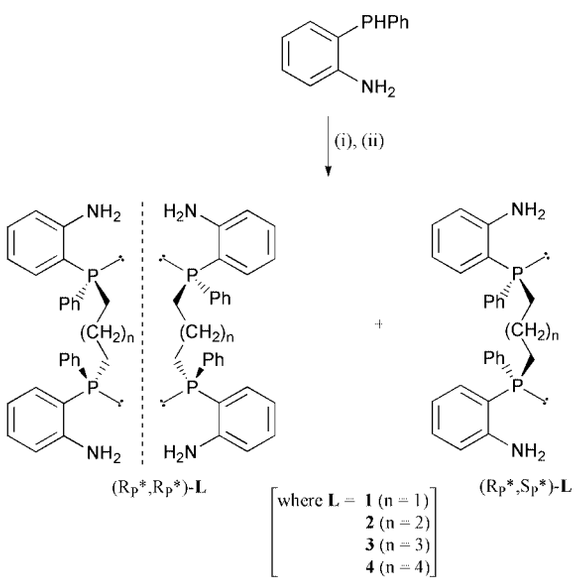
 DOI: 10.1039/b106861j

L = **6** or 1,2-bis[(2-diphenylphosphinophenyl)amino]ethane,[7] **7**] and $[(PtCl_2)_2(\mu\text{-}\mathbf{6})]$ is also described. We have previously used a similar approach to prepare mono(bidentate) complexes of platinum(II) containing bidentate ligands with a stereogenic phosphorus donor atom and a primary amine group.[8] Moreover, these complexes were shown to exhibit antiproliferative activity against the mouse tumour model P815 *in vitro* with cytotoxicities of certain of the complexes being comparable to that of cisplatin, *cis*-$[PtCl_2(NH_3)_2]$. Sadler *et al.* have recently reported on the synthesis of a number of related mononuclear platinum(II) complexes containing achiral bidentate ligands with phosphorus and nitrogen donor atoms that are seen as potential dual-mode anticancer agents.[9] The dinuclear complexes $[(MCl_2)_2(\mu\text{-quadridentate})]$ [where M = Pd(II) or Pt(II)] and $[(PtClMe)_2(\mu\text{-quadridentate})]$ are similarly seen as potential anticancer agents. Accordingly, some preliminary biological results concerning the *in vitro* cytotoxicities of certain of these complexes against the mouse tumour model P388 are also reported. The achiral multinuclear platinum-based compound BBR3464, $[Pt_3Cl_2(NH_3)_5\{\mu\text{-}H_2N(CH_2)_6NH_2\}](NO_3)_4$,[10] is currently undergoing extensive clinical trials.

Results and discussion

Synthesis of quadridentate ligands

The linear quadridentate NPPN ligands **1**,[4] **2**, **3**, and **4** were synthesised by reaction of secondary phosphine (±)-(2-aminophenyl)phenylphosphine[11] with sodium in thf followed by the addition of one-half equivalent of the appropriate dibromoalkane (Scheme 1). All four ligands were isolated as air-stable



Scheme 1 (i) Na, thf; (ii) 0.5 $BrCH_2(CH_2)_nCH_2Br$ (where n = 1–4).

white crystalline solids containing both racemic and meso diastereomers upon recrystallisation from hot methanol. In the case of **1** partial but not complete separation of the (R_P*,R_P*) and (R_P*,S_P*) diastereomers was achieved by this process. The related linear quadridentate NPPN ligand **5** was prepared in a similar manner by reaction of secondary phosphine (±)-(2-aminoethyl)phenylphosphine with sodium in thf followed by the addition of one-half equivalent of 1,3-dibromopropane.[1] The linear quadridentate PNNP ligands **6** and **7** were prepared by a standard metal template approach that involved reaction of the complex *cis*-$[Ni(2\text{-}HNC_6H_4PPh_2)_2]$ with one-half equivalent of 1,3-bis(tolyl-4-sulfonyloxy)propane or 1,2-bis(tolyl-4-sulfonyloxy)ethane, respectively, in toluene.[5,7] The two diastereomeric forms of **5**, (R_P*,R_P*)- and (R_P*,S_P*)-**5**, and the PNNP ligands **6** and **7** are depicted in Fig. 1.

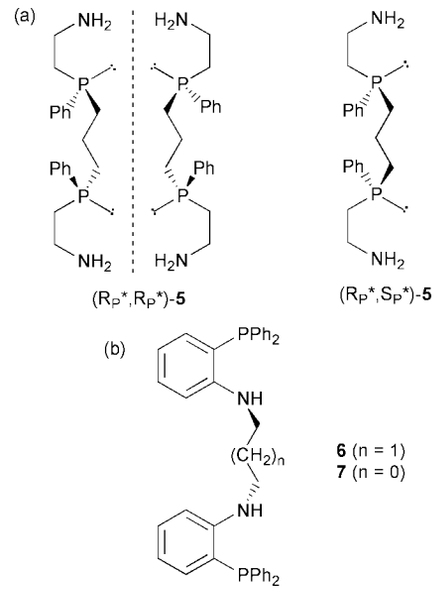


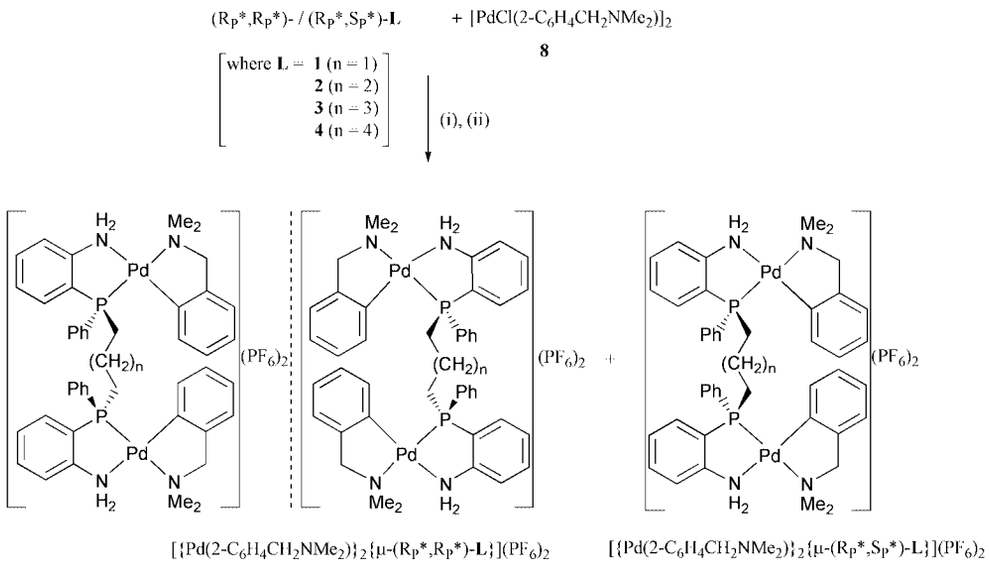
Fig. 1 Stereochemical representation of the linear quadridentate ligands (R_P*,R_P*)-**5**, (R_P*,S_P*)-**5**, **6** and **7**.

Separation of (R_P*,R_P*)- and (R_P*,S_P*)-L

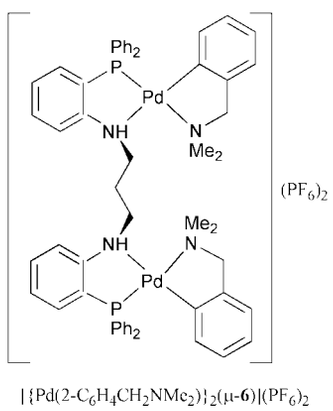
Separation of the (R_P*,R_P*) and (R_P*,S_P*) forms of the five linear quadridentate NPPN ligands was achieved by fractional crystallisation of bis[palladium(II)] complexes containing the respective ligand and orthometallated *N*,*N*-dimethylbenzylamine. For example, reaction of (R_P*,R_P*)-/(R_P*,S_P*)-**1**–**4** with the chloro-bridged dimer di-μ-chloro-bis[2-(dimethylaminomethyl)phenyl-C^1,*N*]dipalladium(II), **8**,[12] in methanol followed by the addition of aqueous ammonium hexafluorophosphate gave a mixture of two diastereomeric salts, *viz.* $[\{Pd(2\text{-}C_6H_4CH_2NMe_2)\}_2(\mu\text{-L})](PF_6)_2$ [where L = (R_P*,R_P*)- or (R_P*,S_P*)-**1**–**4**], that in each case was readily separated by fractional crystallisation from hot methanol (Scheme 2). The related diastereomeric salts $[\{Pd(2\text{-}C_6H_4CH_2NMe_2)\}_2\{\mu\text{-}(R_P^*,R_P^*)\text{-}\mathbf{5}\}](PF_6)_2$ and $[\{Pd(2\text{-}C_6H_4CH_2NMe_2)\}_2\{\mu\text{-}(R_P^*,S_P^*)\text{-}\mathbf{5}\}](PF_6)_2$ were isolated in a similar manner.

Typically an excess of aqueous ammonium hexafluorophosphate was used in the above reactions, however, in the case of ligands **1** and **2**, but not **3**–**5**, it was found to be beneficial to carry out the addition in two steps. The addition of one equivalent of aqueous ammonium hexafluorophosphate to a methanolic solution of **1** and **8** gave a complex containing only (R_P*,R_P*)-**1**. Similar treatment of a methanolic solution of **2** and **8** gave a product enriched in (R_P*,R_P*)-**2**. Further addition of aqueous ammonium hexafluorophosphate to each of these solutions gave a complex enriched in the (R_P*,S_P*) diastereomer of the respective ligand. In each case recrystallisation from hot methanol gave the respective diastereomerically pure complex.

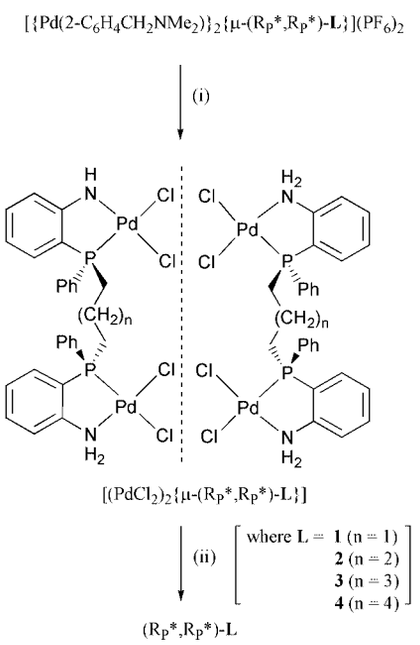
The diastereomerically pure complexes $[\{Pd(2\text{-}C_6H_4CH_2NMe_2)\}_2(\mu\text{-L})](PF_6)_2$ [where L = (R_P*,R_P*)-**1**–**5**, (R_P*,S_P*)-**1**, -**2** or -**5**] have been isolated in the current work. Analogous dipalladium(II) complexes enriched in (R_P*,S_P*)-**3** or -**4** have also been obtained, however, they could not be further separated by fractional crystallisation. The least soluble diastereomeric hexafluorophosphate salt in each case has been assigned the (R_P*,R_P*) configuration based on X-ray analyses of two related complexes containing (R_P,R_P)-**1** and (R_P*,S_P*)-**5**, *viz.* $[(Pd\{(S)\text{-}2\text{-}C_6H_4CHMeNMe_2\})_2\{\mu\text{-}(S_P,S_P)\text{-}\mathbf{1}\}](PF_6)_2$‡ and $[(Pd\{(R)\text{-}2\text{-}C_6H_4CHMeNMe_2\})_2\{\mu\text{-}(R_P^*,S_P^*)\text{-}\mathbf{5}\}](PF_6)_2$, respectively (*vide infra*). The related dinuclear palladium(II) complex $[\{Pd(2\text{-}C_6H_4CH_2NMe_2)\}_2(\mu\text{-}\mathbf{6})](PF_6)_2$ was similarly prepared *via* reaction of **8** with the linear quadridentate PNNP ligand **6** in methanol followed by the addition of aqueous ammonium hexafluorophosphate.



Scheme 2 (i) MeOH; (ii) NH_4PF_6 in H_2O.



Treatment of the diastereomerically pure salts [{Pd(2-$C_6H_4CH_2NMe_2$)}$_2$(μ-L)](PF$_6$)$_2$ [where L = (R_P*,R_P*)-**1**–**4**] with concentrated hydrochloric acid in methanol gave the corresponding bis[dichloropalladium(II)] complexes [(PdCl$_2$)$_2$(μ-L)] (Scheme 3). The related dinuclear dichloropalladium(II) complexes [(PdCl$_2$)$_2${μ-(R_P*,R_P*)-**5**}], [(PdCl$_2$)$_2${μ-(R_P*,S_P*)-L}] (where L = **1**, **2** or **5**) and [(PdCl$_2$)$_2$(μ-**6**)] were prepared in a similar manner. The diastereomerically pure forms of certain of these linear quadridentate NPPN ligands have also been isolated *via* reaction of the appropriate bis[dichloropalladium(II)] complex with aqueous potassium cyanide, namely (R_P*,R_P*)-**1**–**5** and (R_P*,S_P*)-**1** and -**5**.§



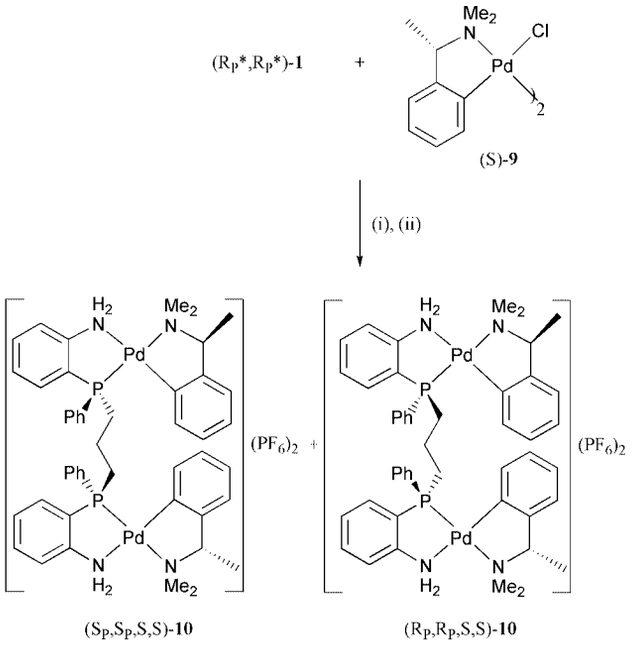
Scheme 3 (i) MeOH, conc. HCl; (ii) MeOH, KCN, CH_2Cl_2, H_2O.

Resolution of (R_P*,R_P*)-1

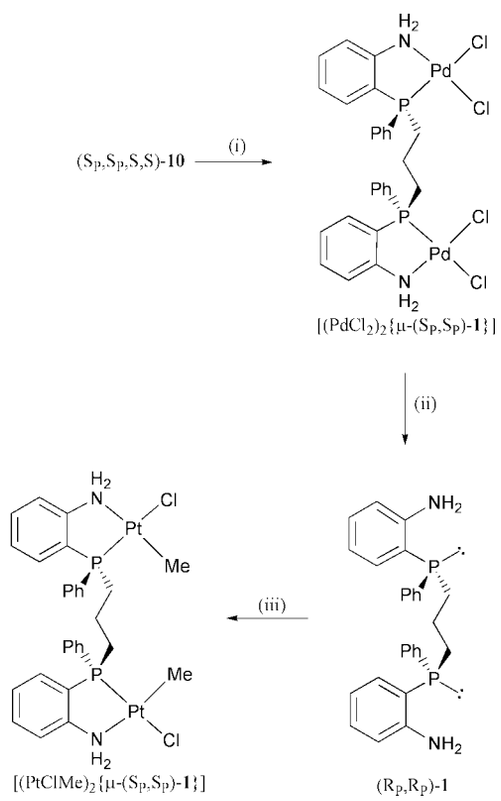
The resolution of (R_P*,R_P*)-**1** has been achieved *via* the separation by fractional crystallisation of a pair of internally diastereomeric dinuclear palladium(II) complexes containing the racemic ligand and optically active, orthometallated (*S*)-dimethyl(1-phenylethyl)amine. Reaction of (R_P*,R_P*)-**1** with the chloro-bridged dimer di-μ-chloro-bis{(*S*)-2-[1-(dimethylamino)ethyl]phenyl-C^1,N}dipalladium(II), (*S*)-**9**,[15] in methanol followed by the addition of an excess of aqueous ammonium hexafluorophosphate gave a 1 : 1 diastereomeric mixture of the bis[palladium(II)] complexes (R_P,R_P,*S*,*S*)- and (S_P,S_P,*S*,*S*)-**10** (Scheme 4). Fractional crystallisation of the diastereomeric mixture from acetone by the dropwise addition of diethyl ether gave pure (S_P,S_P,*S*,*S*)-**10**, α +128° (589 nm, acetone). The mother liquor was taken to dryness and the residue twice recrystallised from acetone–diethyl ether to give pure (R_P,R_P,*S*,*S*)-**10**, α −19° (589 nm, acetone). Subsequent treatment of the diastereomerically pure complex (S_P,S_P,*S*,*S*)-**10** with concentrated hydrochloric acid in hot methanol gave the corresponding optically active bis[dichloropalladium(II)] complex [(PdCl$_2$)$_2$(μ-{(S_P,S_P)-**1**})], α +72° (589 nm, dichloromethane) (Scheme 5). The enantiomeric dinuclear dichloropalladium(II) complex [(PdCl$_2$)$_2$(μ-{(R_P,R_P)-**1**})] was isolated in a similar manner, α −72° (589 nm, dichloromethane). Further reaction of [(PdCl$_2$)$_2$(μ-{(R_P,R_P)-**1**})] and [(PdCl$_2$)$_2$(μ-{(S_P,S_P)-**1**})] with aqueous potassium cyanide gave the enantiomerically pure linear quadridentate NPPN ligands (S_P,S_P)- and (R_P,R_P)-**1**, respectively, α ±65° (589 nm, dichloromethane).

‡ The apparent inversion of configuration at phosphorus upon coordination of (R_P,R_P)-**1** to the palladium(II) centres is consistent with the specification of Cahn *et al.* for absolute configurations.[13]

§ The relative configuration of (R_P*,S_P*)-**5** was determined *via* a crystal structure determination of the complex [(Pd{(*R*)-2-C_6H_4CHMeNMe$_2$}$_2${μ-(R_P*,S_P*)-**5**}](PF$_6$)$_2$.[14] The latter was prepared by reaction of the diastereomerically pure quadridentate ligand with the chloro-bridged dimer (*R*)-**9** in methanol followed by the addition of aqueous NH_4PF_6.



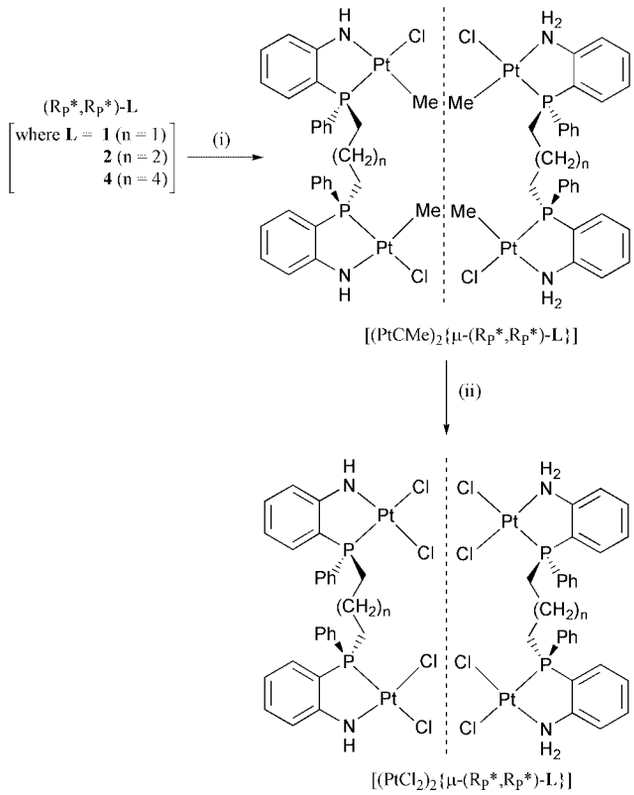
Scheme 4 (i) MeOH; (ii) NH_4PF_6 in H_2O.



Scheme 5 (i) MeOH, conc. HCl; (ii) MeOH, KCN, CH_2Cl_2, H_2O; (iii) [PtCl(Me)(cod)], thf.

Preparation of dinuclear platinum(II) complexes

Dinuclear platinum(II) complexes of the type [$(PtClMe)_2${μ-(R_P*,R_P*)-L}] (where L = **1**, **2** or **4**) have been prepared *via* reaction of the respective racemic quadridentate ligand with two equivalents of [PtCl(Me)(cod)] (where cod = cycloocta-1,5-diene)[16] in thf (Scheme 6). Subsequent treatment of [$(PtClMe)_2${μ-(R_P*,R_P*)-L}] with concentrated hydrochloric acid in methanol gave the corresponding bis[dichloroplatinum(II)] complexes [$(PtCl_2)_2${μ-(R_P*,R_P*)-L}] [where L = **1**, **2** or **4**]. The related dinuclear platinum(II) complexes [$(PtClMe)_2$(μ-L)] [where L = (R_P*,S_P*)-**1**, **6** or **7**] and [$(PtCl_2)_2$(μ-L)] [where L = (R_P*,S_P*)-**1**, (R_P*,R_P*)- or (R_P*,S_P*)-**5** or **6**] were all prepared in



Scheme 6 (i) [PtCl(Me)(cod)], thf; (ii) thf, conc. HCl.

a similar manner. The optically active diplatinum(II) complex [$(PtClMe)_2${μ-(S_P,S_P)-**1**}] was similarly prepared *via* reaction of (R_P,R_P)-**1** with two equivalents of [PtCl(Me)(cod)] in thf (Scheme 5), α +93° (589 nm, dichloromethane). The enantiomeric bis[chloro(methyl)platinum(II)] complex [$(PtClMe)_2${μ-(R_P,R_P)-**1**}] was prepared in a likewise manner, α −93° (589 nm, dichloromethane).

Crystal structure determination of (S_P,S_P,*S*,*S*)-10

The absolute configuration of (R_P,R_P)-**1** was assigned by a crystal structure determination of (S_P,S_P,*S*,*S*)-**10**. The stereochemistry of the cation is depicted in Fig. 2. Selected bond lengths and angles are given in Table 1. The structural data clearly show the presence of a dinuclear palladium(II) cation in which the optically active linear quadridentate ligand is coordinated to both metal centres *via* a stereogenic phosphorus atom and a terminal primary amine group. An optically active, orthometallated dimethyl(1-phenylethyl)amine completes the coordination sphere of each metal centre. The absolute configurations of the two phosphorus stereocentres and the stereogenic carbon atoms of the orthometallated amines were all *S*. Furthermore, the pair of nitrogen atoms coordinated to each of the palladium(II) centres had adopted a *cis* geometry in each case. A similar arrangement of donor atoms was observed in related mononuclear palladium(II) complexes containing an optically active, orthometallated amine and an asymmetric bidentate ligand with both phosphorus and nitrogen donor atoms, *viz.* (R_P)-(2-aminophenyl)(2-chlorophenyl)methylphosphine and (R_P)-methylphenyl(8-quinolyl)phosphine.[15,17] Furthermore, the bond lengths and angles around the two palladium(II) centres in (S_P,S_P,*S*,*S*)-**10** are very similar and comparable to those in the aforementioned mononuclear complexes.

The linear tetra(tertiary phosphine) (R_P*,R_P*)-1,2-bis[(2-diphenylphosphinoethyl)phenylphosphino]ethane has previously been resolved by the method of metal complexation and similarly shown to form a pair of diastereomeric dinuclear palladium(II) complexes upon reaction with (*R*)-**9**.[18] There are

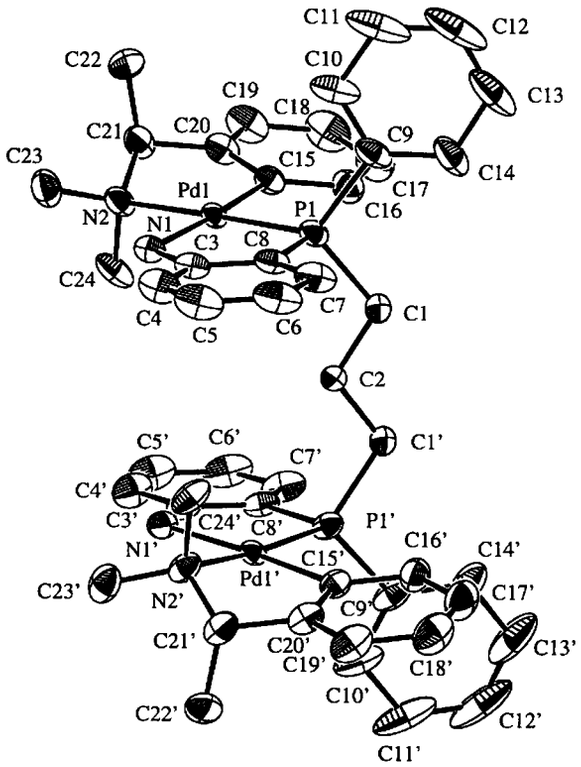


Fig. 2 Molecular structure of the cation (S_P,S_P,S,S)-**10**.

Table 1 Selected non-hydrogen interatomic distances (Å) and interatomic angles (°) for (S_P,S_P,S,S)-**10**

Pd(1)–P(1)	2.206(2)	Pd(1)′–P(1)′	2.207(2)
Pd(1)–N(1)	2.159(6)	Pd(1)′–N(1)′	2.159(6)
Pd(1)–N(2)	2.144(6)	Pd(1)′–N(2)′	2.144(6)
Pd(1)–C(15)	2.007(7)	Pd(1)′–C(15)′	2.006(8)
P(1)–Pd(1)–N(1)	85.5(2)	P(1)′–Pd(1)′–N(1)′	85.2(2)
P(1)–Pd(1)–N(2)	177.7(2)	P(1)′–Pd(1)′–N(2)′	174.0(2)
P(1)–Pd(1)–C(15)	97.2(2)	P(1)′–Pd(1)′–C(15)′	97.4(2)
N(1)–Pd(1)–C(15)	176.8(3)	N(1)′–Pd(1)′–C(15)′	176.5(3)
N(1)–Pd(1)–N(2)	95.4(3)	N(1)′–Pd(1)′–N(2)′	95.9(3)
C(15)–Pd(1)–N(2)	82.0(3)	C(15)′–Pd(1)′–N(2)′	81.9(3)
Pd(1)–P(1)–C(1)	116.6(4)	Pd(1)′–P(1)′–C(1)′	114.2(4)
Pd(1)–P(1)–C(9)	117.9(2)	Pd(1)′–P(1)′–C(9)′	121.5(2)
Pd(1)–P(1)–C(8)	102.9(3)	Pd(1)′–P(1)′–C(8)′	103.2(3)
Pd(1)–N(1)–C(3)	115.6(5)	Pd(1)′–N(1)′–C(3)′	115.8(5)
Pd(1)–C(15)–C(20)	112.6(6)	Pd(1)′–C(15)′–C(20)′	112.3(6)
Pd(1)–C(15)–C(16)	128.8(6)	Pd(1)′–C(15)′–C(16)′	129.2(6)
Pd(1)–N(2)–C(21)	106.9(5)	Pd(1)′–N(2)′–C(21)′	106.0(5)
Pd(1)–N(2)–C(24)	106.1(6)	Pd(1)′–N(2)′–C(24)′	104.8(6)
Pd(1)–N(2)–C(23)	116.3(6)	Pd(1)′–N(2)′–C(23)′	116.2(6)

many similarities between the structures of the diastereomeric complex containing the (S_P,S_P) form of the tetra(tertiary phosphine) and that of (S_P,S_P,S,S)-**10**. For example, in both cases the stereogenic phosphorus centres were *trans* to the dimethylamino group of the orthometallated amine and the methyl substituents of the carbon stereocentres had adopted an axial disposition. The optical antipodes of the tetra(tertiary phosphine) were subsequently shown to spontaneously self-assemble into homochiral double-stranded bimetallic helicates on complexation to gold(I) and silver(I).[18]

NMR spectra

The ^{31}P-{^{1}H} NMR spectra of the optically active dinuclear palladium(II) complexes (S_P,S_P,S,S)- and (R_P,R_P,S,S)-**10**, and of the related diastereomerically pure complexes [{Pd(2-$C_6H_4CH_2NMe_2$)}$_2$(μ-L)](PF$_6$)$_2$ [where L = (R_P*,R_P*)-**1**–**5** or (R_P*,S_P*)-**1**, -**2** or -**5**], each contained a singlet phosphorus resonance consistent with the presence of a single diastereomer. A singlet phosphorus resonance was similarly observed for [{Pd(2-$C_6H_4CH_2NMe_2$)}$_2$(μ-**6**)](PF$_6$)$_2$. Furthermore, the ^{1}H NMR spectra of the complexes containing the linear quadridentate NPPN ligands **1**–**5** are consistent with the solid state structure of (S_P,S_P,S,S)-**10**. For example, coupling of the phosphorus stereocentres to the *trans* disposed NMe groups and the methine protons of (S_P,S_P,S,S)- and (R_P,R_P,S,S)-**10**, or the benzylic protons of [{Pd(2-$C_6H_4CH_2NMe_2$)}$_2$(μ-L)](PF$_6$)$_2$ [where L = (R_P*,R_P*)-**1**–**5** or (R_P*,S_P*)-**1**, -**2** or -**5**], was evident in the respective ^{1}H NMR spectra. A similar finding has previously been reported for mononuclear palladium(II) complexes containing an orthometallated amine and the enantiomers of (±)-(2-aminoethyl)methylphenylphosphine,[19] (±)-(2-aminophenyl)methylphenylphosphine,[11] (±)-(2-aminophenyl)(2-chlorophenyl)methylphosphine[17] and (±)-methylphenyl(8-quinolyl)phosphine.[15] Similar coupling of the phosphorus donor atoms to the *trans* disposed NMe groups and the benzylic protons of the orthometallated amine was evident in the ^{1}H NMR spectrum of [{Pd(2-$C_6H_4CH_2NMe_2$)}$_2$(μ-**6**)](PF$_6$)$_2$. Selected ^{1}H and ^{31}P-{^{1}H} NMR data for the optically active dinuclear palladium(II) complexes (S_P,S_P,S,S)- and (R_P,R_P,S,S)-**10**, the related diastereomerically pure complexes [{Pd(2-$C_6H_4CH_2NMe_2$)}$_2$(μ-L)](PF$_6$)$_2$ [where L = (R_P*,R_P*)-**1**–**5** or (R_P*,S_P*)-**1**, -**2** or -**5**] and [{Pd(2-$C_6H_4CH_2NMe_2$)}$_2$(μ-**6**)](PF$_6$)$_2$ are given in Table 2.

The ^{31}P-{^{1}H} NMR spectra of the related dinuclear complexes [(PdCl$_2$)$_2$(μ-L)] [where L = (R_P,R_P)-, (S_P,S_P)-, (R_P*,R_P*)- or (R_P*,S_P*)-**1**; (R_P*,R_P*)- or (R_P*,S_P*)-**2**; (R_P*,R_P*)-**3**; or (R_P*,R_P*)-**4**], [(PtClMe)$_2$(μ-L)] [where L = (R_P,R_P)-, (S_P,S_P)-, (R_P*,R_P*)- or (R_P*,S_P*)-**1**; (R_P*,R_P*)-**2** or -**4**; or **7**] and [(PtCl$_2$)$_2$(μ-L)] [where L = (R_P*,R_P*)-**1**, (R_P*,S_P*)-**1**, (R_P*,R_P*)-**2** or -**4**] each contained a singlet ^{31}P resonance consistent with the presence of a single diastereomeric complex. Two singlet ^{31}P resonances were observed for the complexes [(PdCl$_2$)$_2$(μ-**6**)], [(PtClMe)$_2$(μ-**6**)] and [(PtCl$_2$)$_2$(μ-**6**)] in their respective ^{31}P-{^{1}H} NMR spectra consistent with the presence of two diastereomers that presumably arise as a result of coordination of the two stereogenic secondary amine groups of the linear quadridentate PNNP ligand **6**. Diastereoisomerism arising from the presence of coordinated chiral secondary amines in kinetically inert transition metal complexes has been well documented.[20–22] The ^{31}P resonances of the dinuclear platinum(II) complexes were also flanked by satellites due to ^{195}Pt–^{31}P coupling, the $^1J_{PtP}$ values of which were consistent with the phosphorus donor atoms being *trans* to chloro groups.[8,23]

Two broad singlet ^{31}P resonances flanked by satellites were similarly observed for the bis[dichloroplatinum(II)] complexes [(PtCl$_2$)$_2$(μ-L)] [where L = (R_P*,R_P*)- or (R_P*,S_P*)-**5**] in their respective ^{31}P-{^{1}H} NMR spectra, however, the chemical shifts of the signals and the associated ^{195}Pt–^{31}P coupling constants in each case were significantly different. Similar data has previously been reported for the monuclear cation [PtCl{(R_P*,R_P*)-**1**}]$^+$ where only one nitrogen atom of the quadridentate ligand was coordinated to the metal centre.[4] The suggestion is that the dinuclear complexes [(PtCl$_2$)$_2$(μ-L)] [where L = (R_P*,R_P*)- or (R_P*,S_P*)-**5**] rearrange in dmso to form mononuclear species of the type [PtCl(L)]$^+$ in which the ligand is similarly coordinated in a tridentate fashion *via* the two phosphorus centres and one nitrogen atom. The upfield signal in each case is assigned to the phosphorus centre *trans* to the chloro group and the other to the phosphorus atom *trans* to the primary amine. The respective $^1J_{PtP}$ values are consistent with this assignment. The analogous bis[dichloropalladium(II)] complexes [(PdCl$_2$)$_2$(μ-L)] [where L = (R_P*,R_P*)- or (R_P*,S_P*)-**5**] were similarly unstable in dmso, the respective ^{31}P-{^{1}H} NMR spectra contained four singlet resonances. The data here are inconsistent with the presence of a single species in solution. Selected ^{1}H and ^{31}P-{^{1}H} NMR data for the quadridentate

Table 2 Selected ^{1}H and ^{31}P-{^{1}H} NMR data for the dinuclear palladium(II) complexes [{Pd(2-$C_6H_4CH_2NMe_2$)}$_2$(μ-L)](PF_6)$_2$ [where L = (R_P*,R_P*)-**1**–**5**, (R_P*,S_P*)-**1**–**5** or **6**], (R_P,R_P,*S*,*S*)- and (S_P,S_P,*S*,*S*)-**10** in $(CD_3)_2CO$

L	^{31}P-{^{1}H} δ(P)	^{1}H δ(CCH_2C)	δ(PCH_2)	δ(NMe_2)	δ(NCH_2)	δ(CH_2NMe_2)[a]
(R_P*,R_P*)-**1**	39.8s	1.93m	2.77m	2.77bs, 2.93d	—	3.60, 4.15
(R_P*,S_P*)-**1**	37.1s	1.75m, 2.22m	2.88m	2.93d, 3.00bs	—	3.78, 4.31
(R_P*,R_P*)-**2**	39.9s	1.47m, 1.97m	2.41m, 2.78m	2.93bs, 3.04bs	—	3.78, 4.48
(R_P*,S_P*)-**2**	38.2s	1.73m, 1.87m	2.42m, 2.68m	2.91bs, 3.01bs	—	3.74, 4.91
(R_P*,R_P*)-**3**	39.5s	1.35m, 1.55m	2.45m, 2.72m	2.95bs, 3.03d	—	3.99, 4.25
(R_P*,R_P*)-**4**	39.0s	1.30m, 1.62m	2.51m, 2.81m	2.94bs, 3.03bs	—	3.81, 4.41
(R_P*,R_P*)-**5**	52.6s	2.15m	2.25m, 2.65m	2.87bs, 2.95bs	3.10m, 3.25m	3.60, 4.61
(R_P*,S_P*)-**5**	51.8s	2.14m	2.34m, 2.61m	2.84bs, 2.89bs	3.05m, 3.15m	3.69, 4.35
6	39.4s	1.98m	—	2.91bs	3.58m	4.09bs

Compound	^{31}P-{^{1}H} δ(P)	^{1}H δ(CMe)	δ(CCH_2C)	δ(PCH_2)	δ(NMe_2)	δ(CH)
(R_P,R_P,*S*,*S*)-**10**	36.8s	1.46d	1.83m	2.73m, 3.12m	2.88d, 2.90bs	3.82dq
(S_P,S_P,*S*,*S*)-**10**	37.5s	1.60d	1.93m	2.81m, 3.19m	2.72bs, 2.90bs	3.82dq

[a] AB part of an ABX spin system unless otherwise indicated.

ligands **1**–**5** and the dinuclear complexes [(MCl_2)$_2$(μ-L)] [where M = Pd(II) and L = **1**–**6** or M = Pt(II) and L = **1**, **2**, **4**, **5** or **7**] and [(PtClMe)$_2$(μ-L)] (where L = **1**, **2**, **4**, **6** or **7**) are given in Table 3.

Preliminary biological studies

The *in vitro* cytotoxicities of the dinuclear complexes [(MCl_2)$_2$-(μ-L)] [where M = Pd(II) and L = **1** or **5** or M = Pt(II) and L = **1**, **2**, **4**, **5** or **6**] and [(PtClMe)$_2$(μ-L)] (where L = **1**, **2**, **4**, **6** or **7**) have been assessed by measuring the effect on proliferation of the murine P388 leukaemia tumour cell line. The IC_{50} values (concentrations resulting in 50% inhibition of labeled thymidine) for these complexes and the reference compound cisplatin are summarised in Table 4. Several of the dinuclear platinum(II) complexes had activities comparable to that of cisplatin. All of the bis[dichloropalladium(II)] complexes and the two dinuclear platinum(II) complexes containing **5** that were tested, however, had significantly lower activities than cisplatin. In addition, a small but significant difference in activity was observed between the two enantiomeric complexes [(PtClMe)$_2${μ-(R_P,R_P)-**1**}] and [(PtClMe)$_2${μ-(S_P,S_P)-**1**}] in keeping with that previously observed for a range of mononuclear platinum(II) complexes containing optically active diamines.[24] The data also suggest a similar level of antiproliferative activity for dinuclear platinum(II) complexes containing linear quadridentate PNNP rather than NPPN ligands.

Conclusion

A general method has been devised for the separation of the racemic and meso diastereomers of linear quadridentate NPPN ligands *via* fractional crystallisation of a pair of dinuclear palladium(II) complexes containing the respective ligand and orthometallated *N*,*N*-dimethylbenzylamine. The diastereomerically pure complexes were readily converted to the analogous bis[dichloropalladium(II)] compounds by reaction with HCl and the ligand diastereomers themselves obtained upon further treatment with aqueous KCN. A similar approach using optically active (*S*)-dimethyl(1-phenylethyl)amine instead of *N*,*N*-dimethylbenzylamine has also provided a viable method of resolution of the linear quadridentate NPPN ligand (R_P*,R_P*)-1,3-bis(2-aminophenyl)phenylphosphino]propane, (R_P*,R_P*)-**1**. A viable synthetic route has also been devised for the preparation of dinuclear platinum(II) complexes containing linear quadridentate P_2N_2 ligands that involves reaction of the respective ligand with two equivalents of [PtCl(Me)(cod)]. Several bis[chloro(methyl)platinum(II)] containing diastereomerically pure linear quadridentate NPPN ligands and the enantiomers of **1**, have been prepared *via* this approach and in certain cases further reacted with HCl to give the analogous bis[dichloroplatinum(II)] complexes. A preliminary study on the *in vitro* cytotoxicities of these complexes against the murine P388 leukaemia tumour cell line has shown that many of the dinuclear platinum(II) complexes have comparable activity to that of cisplatin and clearly indicates that further investigation of their antiproliferative properties is warranted.

Experimental

Procedures and materials

Reactions involving air-sensitive reagents were performed under argon using Schlenk techniques. Solvents were dried and purified by distillation under argon. NMR spectra were recorded on a Varian Gemini II spectrometer operating at 300 MHz (^{1}H) or 121 MHz (^{31}P-{^{1}H}). Chemical shifts are reported as δ values relative to $SiMe_4$ (^{1}H) or 85% H_3PO_4 (^{31}P-{^{1}H}). Optical rotations were measured with an Optical Activity AA-10 or a Perkin-Elmer Model 241 polarimeter on the specified solutions in 1 dm cells at 20 °C. Elemental analyses were performed by staff within the Research School of Chemistry.

The compounds (±)-(2-aminophenyl)phenylphosphine,[11] (R_P*,R_P*)- and (R_P*,S_P*)-1,3-bis[(2-aminoethyl)phenylphosphino]propane, (R_P*,R_P*)- and (R_P*,S_P*)-**5**,[1] di-μ-chloro-bis[2-(dimethylaminomethyl)phenyl-*C*^{1},*N*]dipalladium(II), **8**,[12] 1,3-bis[(2-diphenylphosphinophenyl)amino]propane, **6**,[5] [*SP*-4-2]-chloro(cycloocta-1,5-diene)methylplatinum(II),[16] 1,2-bis[(2-diphenylphosphinophenyl)amino]ethane, **7**,[7] and di-μ-chloro-bis{(*S*)-2-[1-(dimethylamino)ethyl]phenyl-*C*^{1},*N*}dipalladium-(II), (*S*)-**9**,[15] were prepared by literature procedures.

Preparations

(R_P*,R_P*)- and (R_P*,S_P*)-1,3-bis(2-aminophenyl)phenylphosphino]propane, (R_P*,R_P*)- and (R_P*,S_P*)-1. Sodium foil (0.788 g, 0.0343 mol) was added to a solution of (±)-(2-aminophenyl)phenylphosphine (6.90 g, 0.0343 mol) in thf (100 cm^3) and the resulting red solution allowed to stir overnight. The reaction mixture was cooled to −78 °C and a solution of 1,3-dibromopropane (3.46 g, 0.0171 mol) in thf (50 cm^3) added dropwise with stirring. The reaction mixture was allowed to come to ambient temperature and stirred for a further 48 h. An aqueous solution of ammonium chloride (20% w/w, 5 cm^3) was

Table 3 Selected ^{1}H and ^{31}P-{^{1}H} NMR data for the quadridentate ligands L and the dinuclear complexes [$(MCl_2)_2$(μ-L)] [where M = Pd(II) or Pt(II)] and [$(PtClMe)_2$(μ-L)]

	^{31}P-{^{1}H}	^{1}H					
L	δ(P)	δ(Pt*Me*)	δ(CCH_2C)	δ(PCH_2)	δ(NCH_2)	δ(NH_2)	δ(Aromatics)
(a) Ligands [a]							
(R_P*,R_P*)-**1**	−34.9s	—	1.67m	2.21m	—	4.11bs	6.62–7.37m
(R_P,R_P)-**1**	−34.9s	—	1.67m	2.21m	—	4.11bs	6.62–7.37m
(S_P,S_P)-**1**	−34.9s	—	1.67m	2.21m	—	4.11bs	6.62–7.37m
(R_P*,S_P*)-**1**	−35.0s	—	1.70m	2.22m	—	4.12bs	6.60–7.42m
(R_P*,R_P*)-**2**	−34.0s	—	1.59m	2.03m	—	4.12bs	6.63–7.36m
(R_P*,R_P*)-**3** [b]	−34.7s	—	1.46m	2.01m	—	4.38bs	6.63–7.39m
(R_P*,R_P*)-**4**	−33.9s	—	1.42m	2.00m	—	4.10bs	6.63–7.40m
(R_P*,R_P*)-**5** [c]	−30.8s	—	1.46m	1.80m	2.72m	1.46bs	7.11–7.47m
(R_P*,S_P*)-**5** [c]	−30.8s	—	1.46m	1.79m	2.68m	1.46bs	7.25–7.60m
(b) [$(PdCl_2)_2$(μ-L)] [d]							
(R_P*,R_P*)-**1**	47.9s	—	1.78m	2.91m, 3.21m	—	[e]	7.29–7.91m
(R_P,R_P)-**1**	47.9s	—	1.78m	2.91m, 3.21m	—	[e]	7.29–7.91m
(S_P,S_P)-**1**	47.9s	—	1.78m	2.91m, 3.21m	—	[e]	7.29–7.91m
(R_P*,S_P*)-**1**	48.5s	—	1.75m, 2.15m	2.70m, 2.91m	—	[e]	7.41–7.97m
(R_P*,R_P*)-**2**	51.2s	—	1.37m, 2.05m	2.66m	—	[e]	7.42–7.82m
(R_P*,S_P*)-**2**	51.1s	—	1.48m, 2.02m	2.65m	—	[e]	7.39–7.84m
(R_P*,R_P*)-**3**	51.2s	—	1.50m, 1.85m	2.75m	—	[e]	7.67–8.05m
(R_P*,R_P*)-**4**	51.2s	—	1.41m, 1.81m	2.58m	—	[e]	7.41–7.81m
(R_P*,R_P*)-**5**	12.2s, 17.4s 64.7s, 65.3s	—	1.85m, 2.27m	2.70m, 2.82m	3.17m	5.45bs	7.56–8.17m
(R_P*,S_P*)-**5**	9.2s, 18.1s 63.5s, 64.2s	—	1.90m, 2.28m	2.70m, 2.80m	3.18m	5.32bs	7.40–8.25m
6	43.4s, 44.4s	—	1.55m	—	3.03m, 3.90m	[e]	6.99–8.90m
(c) [$(PtCl_2)_2$(μ-L)] [d,f]							
(R_P*,R_P*)-**1**	19.2s(3770)	—	1.77m	2.50m	—	[e]	7.20–8.45m
(R_P*,S_P*)-**1**	19.7s(3888)	—	1.09m	2.75m	—	[e]	7.20–8.40m
(R_P*,R_P*)-**2**	22.0s(3844)	—	1.35m, 2.00m	2.55m, 2.71m	—	[e]	7.35–8.25m
(R_P*,R_P*)-**4**	21.8s(3850)	—	1.24m, 1.38m	2.59m	—	[e]	7.35–8.25m
(R_P*,R_P*)-**5**	32.2bs(3680) −6.4bs(3402)	—	2.05m, 2.32m	2.70m	3.50m	5.80bs	7.53–8.20m
(R_P*,S_P*)-**5**	31.2bs(3860) −8.8bs(3360)	—	2.05m, 2.28m	2.65m, 2.84m	3.35m	5.85bs	7.48–8.33m
6	16.2s(3917) 16.7s(3912)	—	1.44m	—	3.64m	[e]	7.24–9.35m
(d) [$(PtClMe)_2$(μ-L)] [b,f]							
(R_P*,R_P*)-**1**	19.2s(4618)	−0.08s	1.84m	2.57m, 3.39m	—	[e]	6.55–7.83m
(R_P,R_P)-**1**	19.2s(4618)	−0.08s	1.84m	2.57m, 3.39m	—	[e]	6.55–7.83m
(S_P,S_P)-**1**	19.2s(4618)	−0.08s	1.84m	2.57m, 3.39m	—	[e]	6.55–7.83m
(R_P*,S_P*)-**1** [d]	18.6s(4554)	0.30s	2.09m	2.70m	—	[e]	6.50–8.50m
(R_P*,R_P*)-**2**	19.6s(4631)	0.54s	1.49m, 1.73m	2.38m	—	5.72bs	7.09–7.21m
(R_P*,R_P*)-**4** [d]	20.9s(4560)	0.37s	1.15m, 1.38m	2.34m, 2.63m	—	6.76bs	7.29–7.92m
6	19.4s(4670) 20.0s(4696)	0.59d 0.64d	1.76m	—	3.17m 3.83m	[e]	7.01–7.89m
7	19.3s(4769)	0.68s	—	—	2.04m, 4.60m	[e]	7.26–8.17m

[a] In $CDCl_3$. [b] In $(CD_3)_2CO$. [c] In CD_2Cl_2. [d] In $(CD_3)_2SO$. [e] Obscured by the manifold of aromatic resonances. [f] Values of $^1J_{PtP}$ are given in Hz in parentheses.

added and the solvent removed under reduced pressure. Water (75 cm^3) was added to the residue and the solution extracted with dichloromethane (3 × 40 cm^3). The combined organic extracts were dried ($MgSO_4$), filtered and the solvent removed under reduced pressure. The solid residue was recrystallised from hot methanol (100 cm^3) to give a white crystalline mass of (R_P*,R_P*)- and (R_P*,S_P*)-**1**. The product was collected, washed with cold methanol and dried *in vacuo* (3.70 g, 49%). [Batch A] (Found: C, 73.1; H, 6.5; N, 6.0. Calc. for $C_{27}H_{28}N_2P_2$: C, 73.3; H, 6.4, N, 6.3%). ^{1}H NMR ($CDCl_3$): δ 1.67 (m, 2 H, CCH_2C), 2.21 (m, 4 H, PCH_2), 4.11 (bs, 4 H, NH_2), 6.62–7.36 (m, 18 H, aromatics). ^{31}P-{^{1}H} NMR ($CDCl_3$): δ −34.9 (s, 2 P), −35.0 (s, 2 P). *m*/*z*: 442, (M^+); 365, ($M - C_6H_5$)$^+$; 350, ($M - C_6H_5NH_2$)$^+$; 242, ($M - C_6H_5PC_6H_4NH_2$)$^+$. A second crop of crystals was obtained on reducing the volume of the filtrate by *ca.* 50% (2.03 g, 27%). [Batch B]

The following compounds were prepared in a similar manner: (R_P*,R_P*)- and (R_P*,S_P*)-1,4-bis[(2-aminophenyl)phenylphosphino]butane, (R_P*,R_P*)- and (R_P*,S_P*)-**2**; (R_P*,R_P*)- and (R_P*,S_P*)-1,5-bis[(2-aminophenyl)phenylphosphino]pentane, (R_P*,R_P*)- and (R_P*,S_P*)-**3**; and (R_P*,R_P*)- and (R_P*,S_P*)-1,6-bis[(2-aminophenyl)phenylphosphino]hexane, (R_P*,R_P*)- and (R_P*,S_P*)-**4**.

Separation of (R_P*,R_P*)- and (R_P*,S_P*)-L. Formation and separation of the internally diastereomeric complexes [*SP*-4-2-(R_P*,R_P*)]- and [*SP*-4-2-(R_P*,S_P*)]-{μ-1,3-bis[(2-aminophenyl)-phenylphosphino]propane}{bis[2-(dimethylaminomethyl)phenyl-*C*^{1},*N*]}dipalladium(II) hexafluorophosphate-hydrate (1/2), [{Pd-(2-$C_6H_4CH_2NMe_2$)}$_2${μ-(R_P*,R_P*)-1}](PF$_6$)$_2$ and [{Pd(2-C_6H_4-CH_2NMe_2)}$_2${μ-(R_P*,S_P*)-1}](PF$_6$)$_2$. The chloro-bridged dimer di-μ-chloro-bis[2-(dimethylaminomethyl)phenyl-*C*^{1},*N*]dipalladium(II), **8** (4.60 g, 8.33 mmol) and batch A of the linear quadridentate P_2N_2 ligand (R_P*,R_P*)- and (R_P*,S_P*)-**1** (3.69 g, 8.33 mmol) were suspended in methanol (100 cm^3) and the mixture stirred until dissolution was complete. The yellow

Table 4 IC_{50} values for selected dinuclear complexes of the type $[(MCl_2)_2(\mu\text{-L})]$ [where M = Pd(II) or Pt(II)] and $[(PtClMe)_2(\mu\text{-L})]$ against the murine P388 leukaemia tumour cell line

	IC_{50}/μmol dm^{-3} [a]		
L	$[(PtClMe)_2(\mu\text{-L})]$	$[(PtCl_2)_2(\mu\text{-L})]$	$[(PdCl_2)_2(\mu\text{-L})]$
(R_P*,R_P*)-**1**	0.9	65	65
(R_P*,S_P*)-**1**	30	90	70
(R_P,R_P)-**1**	5.6	—	—
(S_P,S_P)-**1**	1.5	—	—
(R_P*,R_P*)-**2**	1.0	0.1	—
(R_P*,R_P*)-**4**	3.4	0.14	—
(R_P*,R_P*)-**5**	—	65	[b]
(R_P*,S_P*)-**5**	—	[b]	[b]
6	0.44	0.12	—
7	1.9	—	—

[a] An IC_{50} value of 1.1 μmol dm^{-3} was obtained for the reference compound *cis*-$[PtCl_2(NH_3)_2]$. [b] The IC_{50} value is >100 μmol dm^{-3} and hence could not be determined from the concentration range used in the assay.

solution was filtered, a solution of ammonium hexafluorophosphate (1.36 g, 8.33 mmol) in water (5 cm^3) was added dropwise and the mixture stirred for 2 h. The resulting white precipitate of diastereomerically pure $[\{Pd(2\text{-}C_6H_4CH_2NMe_2)\}_2\{\mu\text{-}(R_P\text{*},R_P\text{*})\text{-}\mathbf{1}\}](PF_6)_2$ was collected, washed with methanol (2 × 5 cm^3) and dried *in vacuo* (6.14 g, 61%). Complete removal of chloride ion from the sample was achieved by dissolving the complex (0.50 g, 0.412 mmol) in acetone (50 cm^3) followed by the addition of a solution of ammonium hexafluorophosphate to give $[\{Pd(2\text{-}C_6H_4CH_2NMe_2)\}_2\{\mu\text{-}(R_P\text{*},R_P\text{*})\text{-}\mathbf{1}\}](PF_6)_2$ (0.45 g, 90%), mp 226–227 °C. (Found: C, 42.9; H, 4.5; N, 4.5. Calc. for $C_{45}H_{52}F_{12}N_4P_4Pd_2{\cdot}2H_2O$: C, 43.2; H, 4.5; N, 4.5%). ^{1}H NMR $[(CD_3)_2CO]$: δ 1.93 (m, 2 H, CCH_2C), 2.77 (m, 4 H, PCH_2), 2.77 (bs, 6 H, NMe), 2.93 (d, 6 H, $^3J_{PH}$ 9 Hz, NMe), 3.60, 4.15 (bAB q, 4 H, $^2J_{AB}$ 14 Hz, CH_2NMe_2), 6.68 (bs, 4 H, NH_2), 6.93–8.01 (m, 26 H, aromatics). ^{31}P-{^{1}H} NMR $[(CD_3)_2CO]$: δ 39.8 (s, 2 P).

Excess ammonium hexafluorophosphate (2.72 g, 16.7 mmol) in water (15 cm^3) was added dropwise to the filtrate from the isolation of $[\{Pd(2\text{-}C_6H_4CH_2NMe_2)\}_2\{\mu\text{-}(R_P\text{*},R_P\text{*})\text{-}\mathbf{1}\}]X_2$. Water (50 cm^3) was added and the resulting white precipitate enriched in $[\{Pd(2\text{-}C_6H_4CH_2NMe_2)\}_2\{\mu\text{-}(R_P\text{*},S_P\text{*})\text{-}\mathbf{1}\}](PF_6)_2$ was collected, washed with water (5 cm^3), methanol–diethyl ether (1 : 9, 5 cm^3) and finally diethyl ether (5 cm^3) and dried *in vacuo* (3.02 g, 30%). ^{31}P-{^{1}H} NMR $[(CD_3)_2CO]$: δ 37.1 (s, 2 P), 39.8 (s, 2 P).

The above procedure was repeated using batch B of (R_P*,R_P*)- and (R_P*,S_P*)-**1** (2.00 g, 4.51 mmol) and **6** (2.49 g, 4.51 mmol) to give pure $[\{Pd(2\text{-}C_6H_4CH_2NMe_2)\}_2\{\mu\text{-}(R_P\text{*},R_P\text{*})\text{-}\mathbf{1}\}](PF_6)_2$ (0.665 g, 15%) and a hexafluorophosphate salt enriched in $[\{Pd(2\text{-}C_6H_4CH_2NMe_2)\}_2\{\mu\text{-}(R_P\text{*},S_P\text{*})\text{-}\mathbf{1}\}](PF_6)_2$ (2.41 g, 58%).

The meso-enriched hexafluorophosphate salt (5.43 g, 4.5 mmol) was dissolved in hot methanol (200 cm^3), the solution filtered and the volume of filtrate reduced by *ca*. 50% to give diastereomerically pure $[\{Pd(2\text{-}C_6H_4CH_2NMe_2)\}_2\{\mu\text{-}(R_P\text{*},S_P\text{*})\text{-}\mathbf{1}\}](PF_6)_2$ as fine white needles. The complex was collected, washed with methanol–diethyl ether (1 : 9, 5 cm^3) followed by diethyl ether (5 cm^3) and dried *in vacuo* (3.98 g, 73%), mp 250–252 °C. (Found: C, 42.7; H, 4.5; N, 4.4. Calc. for $C_{45}H_{52}F_{12}N_4P_4Pd_2{\cdot}2H_2O$: C, 43.2; H, 4.5; N, 4.5%). ^{1}H NMR $[(CD_3)_2CO]$: δ 1.75 (m, 1 H, CCH*H*C), 2.22 (m, 1 H, CC*H*HC), 2.88 (m, 4 H, PCH_2), 2.93 (d, 6 H, $^3J_{PH}$ 9 Hz, NMe), 3.00 (bs, 6 H, NMe), 3.78, 4.31 (AB part of ABX m, 4 H, $^2J_{AB}$ 14 Hz, $^4J_{AX}$ 3 Hz, $^4J_{BX} \approx 0$ Hz, CH_2NMe_2), 6.62–7.86 (m, 30 H, aromatics and NH_2). ^{31}P-{^{1}H} NMR $[(CD_3)_2CO]$: δ 37.1 (s, 2 P).

The following compounds were prepared and separated in a similar manner: [*SP*-4-2-(R_P*,R_P*)]- and [*SP*-4-2-(R_P*,S_P*)]-{μ-1,4-bis[(2-aminophenyl)phenylphosphino]butane}{bis[2-(dimethylaminomethyl)phenyl-C^1,*N*]}dipalladium(II) hexafluorophosphate-hydrate (1/1), $[\{Pd(2\text{-}C_6H_4CH_2NMe_2)\}_2\{\mu\text{-}(R_P\text{*},R_P\text{*})\text{-}\mathbf{2}\}](PF_6)_2$ and $[\{Pd(2\text{-}C_6H_4CH_2NMe_2)\}_2\{\mu\text{-}(R_P\text{*},S_P\text{*})\text{-}\mathbf{2}\}](PF_6)_2$; [*SP*-4-2-($R_P$*,$R_P$*)]- and [*SP*-4-2-($R_P$*,$S_P$*)]-{μ-1,5-bis[(2-aminophenyl)phenylphosphino]pentane}{bis[2-(dimethylaminomethyl)phenyl-C^1,*N*]}dipalladium(II) hexafluorophosphate, $[\{Pd(2\text{-}C_6H_4CH_2NMe_2)\}_2\{\mu\text{-}(R_P\text{*},R_P\text{*})\text{-}\mathbf{3}\}](PF_6)_2$ and $[\{Pd(2\text{-}C_6H_4CH_2NMe_2)\}_2\{\mu\text{-}(R_P\text{*},S_P\text{*})\text{-}\mathbf{3}\}](PF_6)_2$; [*SP*-4-2-($R_P$*,$R_P$*)]- and [*SP*-4-2-($R_P$*,$S_P$*)]-{μ-1,6-bis[(2-aminophenyl)phenylphosphino]hexane}{bis[2-(dimethylaminomethyl)phenyl-C^1,*N*]}-dipalladium(II) hexafluorophosphate, $[\{Pd(2\text{-}C_6H_4CH_2NMe_2)\}_2\{\mu\text{-}(R_P\text{*},R_P\text{*})\text{-}\mathbf{4}\}](PF_6)_2$ and $[\{Pd(2\text{-}C_6H_4CH_2NMe_2)\}_2\{\mu\text{-}(R_P\text{*},S_P\text{*})\text{-}\mathbf{4}\}](PF_6)_2$; [*SP*-4-2-($R_P$*,$R_P$*)]- and [*SP*-4-2-($R_P$*,$S_P$*)]-{μ-1,3-bis[(2-aminoethyl)phenylphosphino]propane}{bis[2-(dimethylaminomethyl)phenyl-C^1,*N*]}dipalladium(II) hexafluorophosphate-hydrate (1/1), $[\{Pd(2\text{-}C_6H_4CH_2NMe_2)\}_2\{\mu\text{-}(R_P\text{*},R_P\text{*})\text{-}\mathbf{5}\}](PF_6)_2$ and $[\{Pd(2\text{-}C_6H_4CH_2NMe_2)\}_2\{\mu\text{-}(R_P\text{*},S_P\text{*})\text{-}\mathbf{5}\}](PF_6)_2$; and [*SP*-4-2]-{μ-1,3-bis[(2-diphenylphosphinophenyl)amino]propane}{bis[2-(dimethylaminomethyl)phenyl-C^1,*N*]}dipalladium(II) hexafluorophosphate, $[\{Pd(2\text{-}C_6H_4CH_2NMe_2)\}_2(\mu\text{-}\mathbf{6})](PF_6)_2$.

[*SP*-4-2-(R_P*,R_P*)]-{μ-1,3-Bis[(2-aminophenyl)phenylphosphino]propane}bis[dichloropalladium(II)]hydrochloride (2/1), $[(PdCl_2)_2\{\mu\text{-}(R_P\text{*},R_P\text{*})\text{-}\mathbf{1}\}]$. The complex $[\{Pd(2\text{-}C_6H_4CH_2NMe_2)\}_2\{\mu\text{-}(R_P\text{*},R_P\text{*})\text{-}\mathbf{1}\}](PF_6)_2$ (3.12 g, 2.57 mmol) was suspended in methanol (100 cm^3), hydrochloric acid (10 M, 10 cm^3) was added and the solution refluxed overnight. The yellow crystals of $[(PdCl_2)_2\{\mu\text{-}(R_P\text{*},R_P\text{*})\text{-}\mathbf{1}\}]$ that formed were collected, washed with diethyl ether–methanol (9 : 1, 10 cm^3) and dried *in vacuo* (2.02 g, 99%), mp 248 °C (decomp.). (Found: C, 39.9; H, 3.8; N, 3.4. Calc. for $C_{27}H_{28}Cl_4N_2P_2Pd_2{\cdot}0.5HCl$: C, 39.8; H, 3.5, N, 3.4%). ^{1}H NMR $[(CD_3)_2SO]$: δ 1.78 (m, 2 H, CCH_2C), 2.91 (m, 2 H, PC*H*H), 3.21 (m, 2 H, PCH*H*), 7.29–7.91 (m, 22 H, aromatics and NH_2). ^{31}P-{^{1}H} NMR $[(CD_3)_2SO]$: δ 47.9 (s, 2 P).

The following compounds were prepared in a similar manner: [*SP*-4-2-(R_P*,S_P*)]-{μ-1,3-bis[(2-aminophenyl)phenylphosphino]propane}bis[dichloropalladium(II)]hydrochloride (1/1), $[(PdCl_2)_2\{\mu\text{-}(R_P\text{*},S_P\text{*})\text{-}\mathbf{1}\}]$; [*SP*-4-2-($R_P$*,$R_P$*)]-{μ-1,4-bis[(2-aminophenyl)phenylphosphino]butane}bis[dichloropalladium(II)]hydrochloride (1/1), $[(PdCl_2)_2\{\mu\text{-}(R_P\text{*},R_P\text{*})\text{-}\mathbf{2}\}]$; [*SP*-4-2-($R_P$*,$S_P$*)]-{μ-1,4-bis[(2-aminophenyl)phenylphosphino]-butane}bis[dichloropalladium(II)]hydrochloride (1/1), $[(PdCl_2)_2\{\mu\text{-}(R_P\text{*},S_P\text{*})\text{-}\mathbf{2}\}]$; [*SP*-4-2-($R_P$*,$R_P$*)]-{μ-1,5-bis[(2-aminophenyl)phenylphosphino]pentane}bis[dichloropalladium(II)], $[(PdCl_2)_2\{\mu\text{-}(R_P\text{*},R_P\text{*})\text{-}\mathbf{3}\}]$; [*SP*-4-2-($R_P$*,$R_P$*)]-{μ-1,6-bis[(2-aminophenyl)phenylphosphino]hexane}bis[dichloropalladium(II)], $[(PdCl_2)_2\{\mu\text{-}(R_P\text{*},R_P\text{*})\text{-}\mathbf{4}\}]$; [*SP*-4-2-($R_P$*,$R_P$*)]-{μ-1,3-bis[(2-aminoethyl)phenylphosphino]propane}bis[dichloropalladium(II)]hydrochloride (1/3), $[(PdCl_2)_2\{\mu\text{-}(R_P\text{*},R_P\text{*})\text{-}\mathbf{5}\}]$; [*SP*-4-2-($R_P$*,$S_P$*)]-{μ-1,3-bis[(2-aminoethyl)phenylphosphino]propane}bis[dichloropalladium(II)]hydrochloride (2/5), $[(PdCl_2)_2\{\mu\text{-}(R_P\text{*},S_P\text{*})\text{-}\mathbf{5}\}]$; and [*SP*-4-2]-{μ-1,3-bis[(2-diphenylphosphinophenyl)amino]propane}bis[dichloropalladium(II)]-hydrate (1 : 2), $[(PdCl_2)_2(\mu\text{-}\mathbf{6})]$.

(R_P*,R_P*)-1,3-Bis[(2-aminophenyl)phenylphosphino]propane-hydrate (2/1), (R_P*,R_P*)-1. To a suspension of $[(PdCl_2)_2\{\mu\text{-}(R_P\text{*},R_P\text{*})\text{-}\mathbf{1}\}]$ (4.28 g, 5.37 mmol) in methanol (150 cm^3) was added petroleum spirit (bp 40–60 °C) (75 cm^3) and potassium cyanide (3.36 g, 0.0500 mol) and the mixture shaken thoroughly until there was no further change in the colour of the solution. Dichloromethane (100 cm^3) and water (70 cm^3) were added, the mixture shaken and the layers separated. The aqueous layer was extracted with dichloromethane (1 × 50 cm^3). The combined organic extracts were washed with water (1 × 50 cm^3) and the aqueous extract washed with dichloromethane (1 × 30 cm^3). The combined organic extracts were dried ($MgSO_4$), filtered and the solvent removed under reduced pressure. The residue

was recrystallised from hot methanol (100 cm^3) to give (R_P*,R_P*)-**1** as fine white needles. A further crop of (R_P*,R_P*)-**1** was obtained upon reduction of the volume of the mother liquor by *ca.* 70%. The combined product was washed with cold methanol (2 × 5 cm^3) and dried *in vacuo* (1.97 g, 83%), mp 148–150 °C. (Found: C, 72.3; H, 6.2; N, 6.2. Calc. for $C_{27}H_{28}N_2P_2$·0.5H_2O: C, 71.8; H, 6.5, N, 6.2%). ^{1}H NMR ($CDCl_3$): δ 1.67 (m, 2 H, CCH_2C), 2.21 (m, 4 H, PCH_2), 4.11 (bs, 4 H, NH_2), 6.62–7.37 (m, 18 H, aromatics). ^{31}P-{^{1}H} NMR ($CDCl_3$): δ −34.9 (s, 2 P).

The following compounds were prepared in a similar manner: (R_P*,S_P*)-1,3-bis[(2-aminophenyl)phenylphosphino]propane-hydrate (2/1), (R_P*,S_P*)-**1**; (R_P*,R_P*)-1,4-bis[(2-aminophenyl)-phenylphosphino]butane, (R_P*,R_P*)-**2**; (R_P*,R_P*)-1,5-bis[(2-aminophenyl)phenylphosphino]pentane, (R_P*,R_P*)-**3**; (R_P*,R_P*)-1,6-bis[(2-aminophenyl)phenylphosphino]hexane, (R_P*,R_P*)-**4**; (R_P*,R_P*)-1,3-bis[(2-aminoethyl)phenylphosphino]propane, (R_P*,R_P*)-**5**; and (R_P*,S_P*)-1,3-bis[(2-aminoethyl)phenyl-phosphino]propane, (R_P*,S_P*)-**5**.

Resolution of (R_P*,R_P*)-1. Formation and separation of the internally diastereomeric complexes [*SP*-4-2-(R_P,R_P,*S*,*S*)]- and [*SP*-4-2-(S_P,S_P,*S*,*S*)]-{μ-1,3-bis[(2-aminophenyl)phenylphosphino]propane}{bis[2-(1-dimethylaminoethyl)phenyl-*C*^{1},*N*}dipalladium(II) hexafluorophosphate, (R_P,R_P,*S*,*S*)- and (S_P,S_P,*S*,*S*)-10. The optically active, chloro-bridged dimer di-μ-chloro-bis-{(*S*)-2-[1-(dimethylamino)ethyl]phenyl-*C*^{1},*N*}dipalladium(II), (*S*)-**9** (2.49 g, 4.29 mmol) and (R_P*,R_P*)-**1** (1.90 g, 4.29 mmol) were suspended in methanol (100 cm^3) and the mixture stirred until dissolution was complete. The yellow solution was filtered and excess ammonium hexafluorophosphate (2.18 g, 13.4 mmol) in water (20 cm^3) was added dropwise followed by the dropwise addition of water (40 cm^3). The resulting white precipitate was isolated by filtration, washed with cold methanol (5 cm^3) and dried *in vacuo* (4.67 g, 87%). ^{31}P-{^{1}H} NMR [$(CD_3)_2CO$]: δ 36.8 (s, 1 P), 37.5 (s, 2 P). The diastereomeric mixture of hexafluorophosphate salts (4.54 g, 3.66 mmol) was dissolved in the minimum volume of acetone (120 cm^3) and diethyl ether (25 cm^3) was added dropwise to give white prisms of (S_P,S_P,*S*,*S*)-**10**. The complex was collected, washed with diethyl ether (2 × 2 cm^3) and dried *in vacuo* (1.34 g, 59%), mp 203 °C (decomp.), α +128° (589 nm, *c* 0.307 g per 100 cm^3, acetone). (Found: C, 45.1; H, 4.9; N, 4.3. Calc. for $C_{47}H_{56}F_{12}N_4P_4Pd_2$: C, 45.5; H, 4.5, N, 4.5%). ^{1}H NMR [$(CD_3)_2CO$]: δ 1.60 (d, 6 H, $^3J_{HH}$ 6.5 Hz, CMe), 1.93 (m, 2 H, CCH_2C), 2.72 (bs, 6 H, NMe), 2.81 (m, 2 H, PC*H*H), 2.90 (bs, 6 H, NMe), 3.19 (m, 2 H, PCH*H*), 3.82 (dq, 2 H, $^3J_{HH}$ 6.5 Hz, $^4J_{PH}$ 6.5 Hz, C*H*Me), 6.71–7.96 (m, 30 H, aromatics and NH_2). ^{31}P-{^{1}H} NMR [$(CD_3)_2CO$]: δ 37.5 (s, 2 P).

The filtrate from the isolation of (S_P,S_P,*S*,*S*)-**10** was evaporated to dryness and re-dissolved in acetone (16 cm^3). Diethyl ether (30 cm^3) was added dropwise to give a product enriched in (R_P,R_P,*S*,*S*)-**10** (1.23 g). The isolated complex was again dissolved in acetone (12 cm^3) and diethyl ether (15 cm^3) added dropwise to give white needles of pure (R_P,R_P,*S*,*S*)-**10** (1.03 g, 45%), mp 212 °C (decomp.), α −19° (589 nm, *c* 0.310 g per 100 cm^3, acetone). (Found C, 45.6; H, 4.4; N, 4.2. Calc. for $C_{47}H_{56}F_{12}N_4P_4Pd_2$: C, 45.5; H, 4.5, N, 4.5%). ^{1}H NMR [$(CD_3)_2CO$]: δ 1.46 (d, 6 H, $^3J_{HH}$ 6.5 Hz, CMe), 1.83 (m, 2 H, CCH_2C), 2.73 (m, 2 H, PC*H*H), 2.88 (d, 6 H, $^4J_{PH}$ 6 Hz, NMe), 2.90 (bs, 6 H, NMe), 3.12 (m, 2 H, PCH*H*), 3.82 (dq, 2 H, $^3J_{HH}$ 6.5 Hz, $^4J_{PH}$ 6 Hz, C*H*Me), 6.59–7.98 (m, 30 H, aromatics and NH_2). ^{31}P-{^{1}H} NMR [$(CD_3)_2CO$]: δ 36.8 (s, 2 P).

[*SP*-4-2-(R_P,R_P)]-{μ-1,3-Bis[(2-aminophenyl)phenylphosphino]propane}bis[dichloropalladium(II)]hydrate (1/1), [$(PdCl_2)_2$-{μ-(R_P,R_P)-1}]. Prepared in a similar manner to [$(PdCl_2)_2${μ-(R_P*,R_P*)-**1**}] except using (R_P,R_P,*S*,*S*)-**10** (0.90 g, 0.72 mmol) to give yellow crystals of [$(PdCl_2)_2${μ-(R_P,R_P)-**1**}] (0.50 g, 87%), mp 248 °C (decomp.), α −72° (589 nm, *c* 0.306 g per 100 cm^3, CH_2Cl_2). (Found: C, 39.5; H, 3.7; N, 3.5. Calc. for $C_{27}H_{28}Cl_4N_2P_2Pd_2$·$H_2O$: C, 39.8; H, 3.7; N, 3.4%). ^{1}H and ^{31}P-{^{1}H}-NMR: identical to that of [$(PdCl_2)_2${μ-(R_P*,R_P*)-**1**}].

[*SP*-4-2-(S_P,S_P)]-{μ-1,3-Bis[(2-aminophenyl)phenylphosphino]-propane}bis[dichloropalladium(II)]hydrochloride (1/1), [$(PdCl_2)_2$-{μ-(S_P,S_P)-1}]. Prepared in a similar manner to [$(PdCl_2)_2${μ-(R_P*,R_P*)-**1**}] except using (S_P,S_P,*S*,*S*)-**10** (1.24 g, 1.0 mmol) to give yellow crystals of [$(PdCl_2)_2${μ-(S_P,S_P)-**1**}] (0.65 g, 82%), mp 248 °C (decomp.), α +72° (589 nm, *c* 0.123 g per 100 cm^3, CH_2Cl_2). (Found C, 38.6; H, 3.5; N, 3.1. Calc. for $C_{27}H_{28}Cl_4N_2P_2Pd_2$·HCl: C, 38.9; H, 3.5; N, 3.4%). ^{1}H and ^{31}P-{^{1}H}-NMR: identical to that of [$(PdCl_2)_2${μ-(R_P*,R_P*)-**1**}].

(R_P,R_P)-1,3-Bis(2-aminophenyl)phenylphosphino]propane, (R_P,R_P)-1. Prepared in a similar manner to (R_P*,R_P*)-**1** except using [$(PdCl_2)_2${μ-(S_P,S_P)-**1**}] (0.40 g, 0.50 mmol) to give white crystals of (R_P,R_P)-**1** (0.22 g, 97%), mp 149–150 °C, α +65° (589 nm, *c* 0.305 g per 100 cm^3, CH_2Cl_2). ^{1}H and ^{31}P-{^{1}H}NMR: identical to that of (R_P*,R_P*)-**1**.

(S_P,S_P)-1,3-Bis(2-aminophenyl)phenylphosphino]propane, (S_P,S_P)-1. Prepared in a similar manner to (R_P*,R_P*)-**1** except using [$(PdCl_2)_2${μ-(R_P,R_P)-**1**}] (0.31 g, 0.39 mmol) to give white crystals of (S_P,S_P)-**1** (0.15 g, 85%), mp 149–150 °C, α −65° (589 nm, *c* 0.306 g per 100 cm^3, CH_2Cl_2). ^{1}H and ^{31}P-{^{1}H}NMR: identical to that of (R_P*,R_P*)-**1**.

[*SP*-4-2-(R_P*,R_P*)]-{μ-1,3-Bis[(2-aminophenyl)phenylphosphino]propane}bis[chloromethylplatinum(II)], [$(PtClMe)_2${μ-(R_P*,R_P*)-1}]. To a solution of (R_P*,R_P*)-**1** (0.08 g, 0.181 mmol) in thf (5 cm^3) was added a solution of [PtClMe(cod)] (0.13 g, 0.362 mmol). Petroleum spirit (bp 40–60 °C) (20 cm^3) was added and the resulting white precipitate of [$(PtClMe)_2${μ-(R_P*,R_P*)-**1**}] was collected, washed with petroleum spirit (5 cm^3) and diethyl ether (5 cm^3) and dried *in vacuo* (0.13 g, 77%), mp 244 °C (decomp.). ^{1}H NMR (CD_2Cl_2): δ −0.08 (s, 6 H, $^2J_{PtH}$ 78 Hz, PtMe), 1.84 (m, 2 H, CCH_2C), 2.57 (m, 2 H, PC*H*H), 3.39 (m, 2 H, PCH*H*), 6.55–7.83 (m, 22 H, aromatics and NH_2). ^{31}P-{^{1}H} NMR (CD_2Cl_2): δ 19.2 (s, 2 P, $^1J_{PtP}$ 4618 Hz).

The following compounds were prepared in a similar manner: [*SP*-4-2-(R_P*,S_P*)]-{μ-1,3-bis[(2-aminophenyl)phenylphosphino]propane}bis[chloromethylplatinum(II)], [$(PtClMe)_2${μ-(R_P*,S_P*)-**1**}]; [*SP*-4-2-(R_P,R_P)]-{μ-1,3-bis[(2-aminophenyl)-phenylphosphino]propane}bis[chloromethylplatinum(II)]hydrate (1/1), [$(PtClMe)_2${μ-(R_P,R_P)-**1**}]; [*SP*-4-2-(S_P,S_P)]-{μ-1,3-bis[(2-aminophenyl)phenylphosphino]propane}-bis[chloromethylplatinum(II)]tetrahydrofuran (2/1), [$(PtClMe)_2${μ-(S_P,S_P)-**1**}]; [*SP*-4-2-(R_P*,R_P*)]-{μ-1,4-bis[(2-aminophenyl)-phenylphosphino]butane}bis[chloromethylplatinum(II)]hydrate (1/2), [$(PtClMe)_2${μ-(R_P*,R_P*)-**2**}]; [*SP*-4-2-(R_P*,R_P*)]-{μ-1,6-bis[(2-aminophenyl)phenylphosphino]hexane}bis[chloromethylplatinum(II)]hydrate (1/1), [$(PtClMe)_2${μ-(R_P*,R_P*)-**4**}]; [*SP*-4-2]-{μ-1,3-bis[(2-diphenylphosphinophenyl)amino]propane}bis[chloromethylplatinum(II)]hydrate (1/3), [$(PtClMe)_2$(μ-**6**)]; and [*SP*-4-2]-{μ-1,2-bis[(2-diphenylphosphinophenyl)-amino]ethane}bis[chloromethylplatinum(II)]hydrate (1 : 2), [$(PtClMe)_2$(μ-**7**)].

[*SP*-4-2-(R_P*,R_P*)]-{μ-1,3-Bis[(2-aminophenyl)phenylphosphino]propane}bis[dichloroplatinum(II)]tetrahydrofuran (2/1), [$(PtCl_2)_2${μ-(R_P*,R_P*)-1}]. An excess of hydrochloric acid (10 M, 5 cm^3) was added to a suspension of [$(PtClMe)_2${μ-(R_P*,R_P*)-**1**}] (0.08 g, 0.0857 mmol) in thf (10 cm^3) and the mixture stirred overnight. Water (10 cm^3) was added and the solution stirred for 30 min. The resulting white precipitate of [$(PtCl_2)_2${μ-(R_P*,R_P*)-**1**}] was collected, washed with diethyl

ether (5 cm^3) and dried *in vacuo* (0.06 g, 75%), mp 263 °C (decomp.). (Found: C, 34.4; H, 3.3; N, 3.0. Calc. for $C_{27}H_{28}Cl_4N_2P_2Pt_2 \cdot 0.5C_4H_8O$: C, 34.5; H, 3.2; N, 2.8%). ^{1}H NMR [$(CD_3)_2SO$]: δ 1.77 (m, 4 H, CCH_2C and thf), 2.50 (m, 4 H, PCH_2), 3.60 (m, 2 H, thf), 7.20–8.45 (m, 22 H, aromatics and NH_2). ^{31}P-{^{1}H} NMR [$(CD_3)_2SO$]: δ 19.2 (s, 2 P, $^1J_{PtP}$ 3770 Hz).

The following compounds were prepared in a similar manner: [*SP*-4-2-(R_P*,S_P*)]-{μ-1,3-bis[(2-aminophenyl)phenylphosphino]propane}bis[dichloroplatinum(II)], [$(PtCl_2)_2${μ-(R_P*,S_P*)-**1**}]; [*SP*-4-2-(R_P*,R_P*)]-{μ-1,4-bis[(2-aminophenyl)-phenylphosphino]butane}bis[dichloroplatinum(II)]tetrahydrofuran (2/1), [$(PtCl_2)_2${μ-(R_P*,R_P*)-**2**}]; [*SP*-4-2-(R_P*,R_P*)]-{μ-1,6-bis[(2-aminophenyl)phenylphosphino]hexane}bis[dichloroplatinum(II)]tetrahydrofuran (2/3), [$(PtCl_2)_2${μ-(R_P*,R_P*)-**4**}]; [*SP*-4-2-(R_P*,R_P*)]-{μ-1,3-bis[(2-aminoethyl)phenylphosphino]-propane}bis[dichloroplatinum(II)]hydrate (1/4), [$(PtCl_2)_2${μ-(R_P*,R_P*)-**5**}]; [*SP*-4-2-(R_P*,S_P*)]-{μ-1,3-bis[(2-aminoethyl)-phenylphosphino]propane}bis[dichloroplatinum(II)]tetrahydrofuran (2/1), [$(PtCl_2)_2${μ-(R_P*,S_P*)-**5**}]; and [*SP*-4-2]-{μ-1,3-bis[(2-diphenylphosphinophenyl)amino]propane}bis[dichloroplatinum(II)]tetrahydrofuran (1/1), [$(PtCl_2)_2$(μ-**6**)].

X-Ray crystallography

Crystal data for complex (S_P,S_P,*S*,*S*)-10. $C_{51.5}H_{65}Cl_{0.5}F_9N_4O_{1.5}P_{3.5}Pd_2$, M = 1274.07, orthorhombic, a = 17.622(4), b = 21.207(3), c = 16.001(3) Å, U = 5980(3) Å^3, T = 193 K, space group $P2_12_12$ (no. 18), Z = 4, μ(Cu-Kα) = 65.1 cm^{-1}, 9587 reflections measured, 8883 unique (R_{int} = 0.066) which were used in all calculations. The final R and R' values on 7442 reflections with $I > 3\sigma(I)$ being 0.060 and 0.112 for constrained refinement using 260 variables.

The data were collected using a Rigaku AFC6R diffractometer at −80 °C. The starting structure was determined by direct methods.[25] The structure exhibits pseudo symmetry and is a displacive modulation of a *I*222 parent structure. There is also disorder of the PF_6^- anions and one acetone molecule. Calculations were performed using the TEXSAN and RAELS96 crystallographic software packages.[26,27] Details of the disorder, pseudo symmetry and refinement are given in the CIF.

CCDC reference number 169728.

See http://www.rsc.org/suppdata/dt/b1/b106861j/ for crystallographic data in CIF or other electronic format.

Biological procedures and materials

P388 leukaemia cells were cultured in Dulbecco's Modified Eagle Medium H16 with 10% horse serum (herein EC10). All cells were cultured and incubated in a Froma Scientific Infrared CO_2 incubator at 37 °C in 5% CO_2. Cell suspensions were centrifuged using a Jouan centrifuge model CR 4 22. Linbro 96 round bottom cell tissue culture plates were used for the thymidine incorporation assay. Cells were harvested using a Pharmacia Version 1.02 Micro Cell Harvester and incorporated thymidine was counted using a Pharmacia 1205 Betaplate liquid scintillation counter. Thymidine incorporation assays were performed following a literature procedure,[28] the compounds tested being dissolved in dimethylsulfoxide (0.2 cm^3) to give a concentration of 0.02 mol dm^{-3} and then diluted to 2×10^{-5} mol dm^{-3} using EC10.

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