Chiral palladium bis(phosphite) *PCP*-pincer complexes *via* ligand C–H activation†

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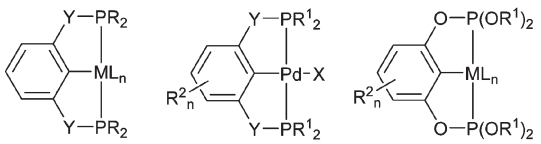
The synthesis of a range of chiral palladium bis(phosphite) pincer complexes has been achieved *via* C–H activation of the parent ligands and one of the complexes formed shows good activity in the catalytic allylation of aldehydes.

The *PCP*-pincer complexes of the general type **1** display a wide range of catalytic activities.[1] For instance, palladium bis(phosphine) pincer complexes (**2**: Y = CH_2) have been used for Heck coupling,[2] whilst bis(phosphinite) complexes (**2**: Y = O) are found to be very active in both Heck and Suzuki reactions.[3,4] Szabó and co-workers recently demonstrated that the bis(phosphinite) pincer complex **2a** (Y = O; R^1 = Ph, R^2 = H; X = TFA) is an excellent catalyst for the reaction of allyl tin reagents with aldehydes and electron-deficient imines.[5] They also found this complex enables the use of potassium trifluoro(allyl) borates as the nucleophiles in the allylation of tosylimines.[6]

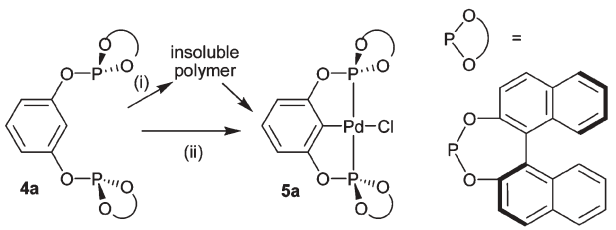


By contrast, there are very few reports on the synthesis and applications of metal *PCP*-bis(*phosphite*) complexes **3**. This is because *PCP*-pincer complexes are typically prepared by C–H activation of the 2-position of the parent ligand and such processes do not seem to be facile for bis(phosphite) pincer ligands. Thus Tilley, Bergman and co-workers showed that the reaction of [{RhCl(COD)}$_2$] with chiral bis(phosphite) pincer ligands gives *cis*-A-frame complexes with bridging bis(phosphite) ligands rather than C–H activation products.[7] Similarly, Nifantyev and co-workers showed that a simple resorcinolbis(phosphite) acts as a non-C–H activated bridging ligand for both rhodium and platinum.[8] To the best of our knowledge the only pincer bis(phosphite) complexes reported are palladium species prepared by the oxidative addition of C–I bonds of 2-iodoresorcinol bis(phosphites).[9]

A simple synthetic route to palladium bis(phosphite) pincer complexes is highly desirable since such species would be more electron-deficient than bis(phosphine) and bis(phosphinite) analogues and should consequently be better Lewis-acid catalysts than their more electron-rich counterparts. We were interested to see whether simple C–H activation routes could be realised and in particular, we were keen to produce chiral complexes for use as catalysts in asymmetric, Lewis acid-catalysed reactions. The preliminary results of this study which are presented below show that this is indeed achievable.

The thermal reactions of ligand (*R*)-**4a**[7]‡ with dichloropalladium(II)-containing precursors in a range of solvents for short periods (< 1 day) do not yield the desired monomeric pincer complex **5a** but instead give insoluble polymeric species. This is presumably a consequence of the ligand's propensity to bridge metal centres.[7] Indeed complex **5a** is only formed after heating ligand **4a** and [$PdCl_2$(NCPh)$_2$] in 1,2-dichloroethane (DCE) for 6 days; the formation of the product is accompanied by the eventual dissolution of the polymeric material (Scheme 1). The reaction rate was enormously enhanced under microwave heating, with good yields of complex **5a** obtained within one hour using DCE as solvent. The ^{31}P NMR spectrum of complex **5a** shows a singlet at 147.2 ppm, close in shift to the free ligand (144.7 ppm). The resonance is significantly to high frequency of simple bis(triarylphosphite)palladium(II) complexes, consistent with *ortho* C–H activation.[10]

Orthometallation of phosphite ligands can be accelerated by the introduction of bulky substituents on the aromatic ring. For example, triarylphosphite ligands with 2-*tert*-butyl groups readily undergo orthopalladation.[10] We reasoned that the incorporation of *tert*-butyl groups into the 4- and 6-positions of resorcinol would not only increase the rate of orthometallation, but that the steric



Scheme 1 *Reagents and conditions*: (i) [$PdCl_2$(NCPh)$_2$], DCE, reflux, 6 d, 77%. (ii) [$PdCl_2$(NCMe)$_2$], μν, 300 W, 150 °C, 1 h, 92%.

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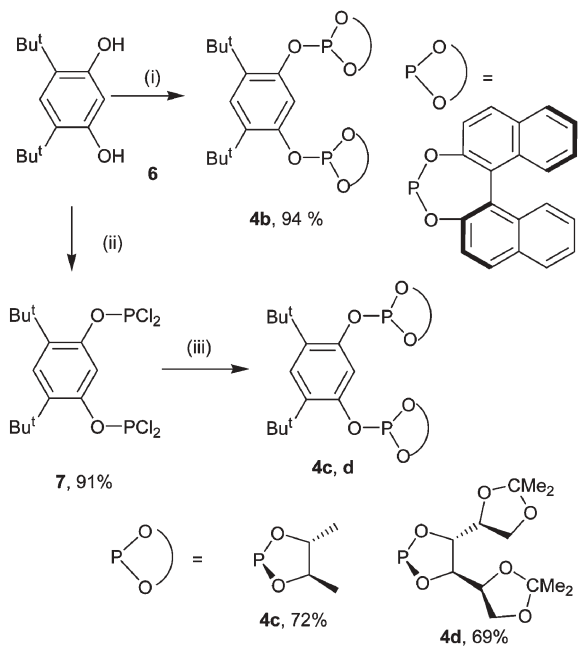
† Electronic supplementary information (ESI) available: Synthesis of ligands and complexes, structure of **5a** and CIF files. See DOI: 10.1039/b609704a

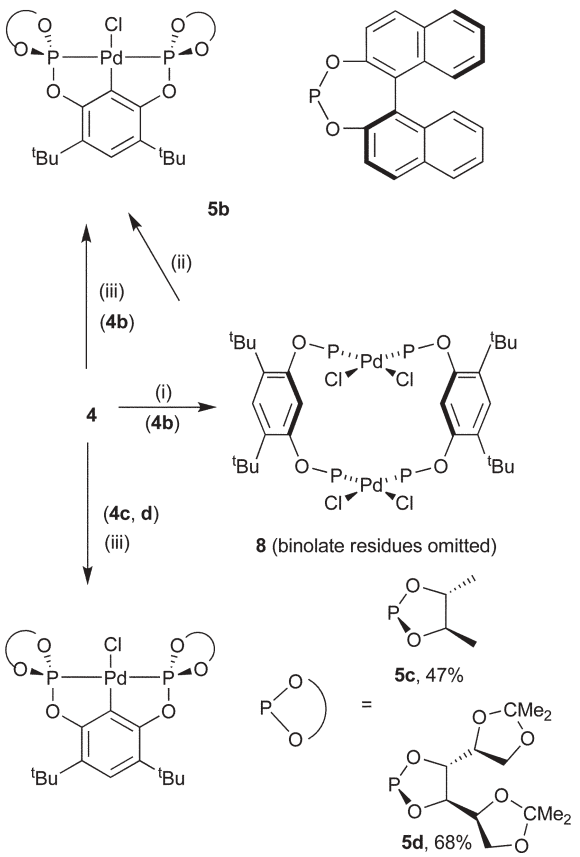


Scheme 2 *Reagents and conditions*: (i) 4-chlorodinaphtho[2,1-*d*:1′,2′-*f*][1,3,2]dioxaphosphepine, THF *or* toluene, Et_3N, −40 °C, 1 h, r.t., 18 h. (ii) PCl_3, NEt_3, toluene, −40 °C to r.t., 18 h. (iii) Chiral diol, Et_3N, toluene,−40 °C to r.t., 18 h.

bulk should limit rotation around the C–O and O–P bonds. This should reduce the chances of insoluble polymer formation, caused by the ligand adopting a bridging mode, and instead favour the formation of monomeric species. Furthermore the bulky substituents may lead to increased enantioselectivity in asymmetric reactions as a result of restricted motion of the BINOL moieties.

Accordingly the ligand (*S*)-**4b** was prepared by the reaction of 4-chlorodinaphtho[2,1-*d*:1′,2′-*f*][1,3,2]-dioxaphosphepine with the di-^{t}Bu-substituted resorcinol **6** (Scheme 2).§ The synthesis of ligand **4c** by this method is not clean; instead it was produced by reaction of the bis(dichlorophosphite), **7**, with (2*R*,3*R*)-(−)-2,3-butanediol. The ligand **4d** was prepared in an analogous fashion.

As anticipated, the more hindered di-*tert*-butylresorcinol-based ligand **4b** does not lead to polymer formation on heating it with $[PdCl_2(NCMe)_2]$ in DCE at reflux temperature but instead, the binuclear complex **8** is formed. This complex can also be produced in CH_2Cl_2 at room temperature. The ^{31}P NMR spectrum of complex **8** shows an AB coupling pattern with doublets at 101.9 and 102.9 ppm (J = 45 Hz). In addition to more typical aromatic residues, the ^{1}H NMR spectrum shows a broad apparent doublet at 5.91 ppm. These spectroscopic data are remarkably similar to those reported for rhodium A-frame complexes with bridging resorcinol bis(phosphite) ligands.[7] The structure of complex **8** was confirmed by X-ray analysis and the molecule is shown in Fig. 1.‖ The 2-Hs of the resorcinol backbones sit in the pseudo-C_2-symmetric cavity between the palladium coordination planes, which presumably accounts for the unusual aromatic environment seen in the ^{1}H NMR spectrum. There is a relatively short contact between each resorcinol 2-H and adjacent palladium centres of approx 2.9 Å (average), about 0.1 Å outside the combined van der Waals radii. Treatment of **8** with triethylamine in dichloromethane at room temperature or toluene at 100 °C gives the desired cyclometallated complex **5b** (Scheme 3). Complex **5b** can also be



Scheme 3 *Reagents and conditions*: (i) $[PdCl_2(NCMe)_2]$, CH_2Cl_2, r.t., 30 min. (ii) NEt_3, toluene, 100 °C, 1 h. (iii) $[PdCl_2(NCMe)_2]$, ligand **4**, NEt_3, 1,2-dichloroethane, 80 °C, 2 h.

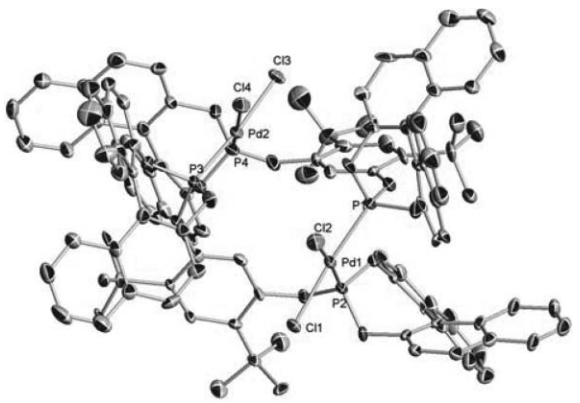


Fig. 1 Crystal structure of complex **8**; ellipsoids set at 30% probability.

prepared directly from ligand **4b** and $[PdCl_2(NCMe)_2]$ in the presence of triethylamine,§ and complexes **5c** and **d** can be prepared in a similar manner.

The X-ray structures of both complexes **5a** and **b** have been determined and the molecular structure of one (**5b**) is shown in Fig. 2.¶‖ The structures of **5a** and **b** are broadly similar with little variation in bond lengths and angles about the square planar palladium centres.

We next examined the use of the complexes **5** in the allylation of benzaldehyde with allyltributyltin (eqn. 1). Szabó and co-workers recently demonstrated that complex **2a** is an excellent catalyst for

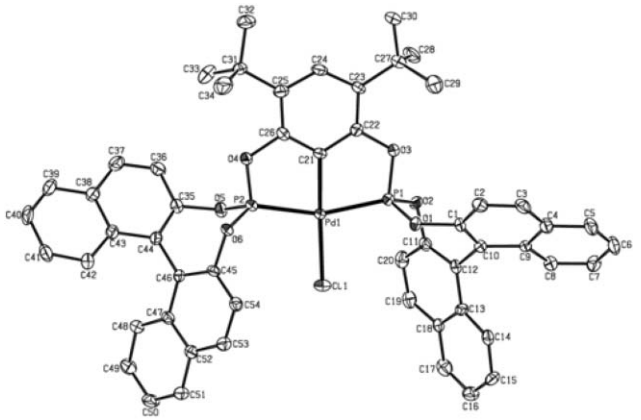
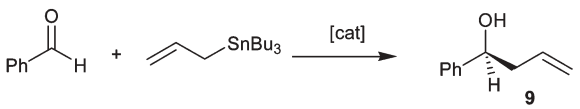


Fig. 2 Crystal structure of complex **5b**. 30% probability. Selected bond lengths (Å) and angles (°): Pd1–C21, 2.003(3); Pd1–P1, 2.2309(9); Pd1–P2, 2.2372(10); Pd1–Cl1, 2.3342(9); C21–Pd1–Cl1, 177.16(10); P1–Pd1–P2, 159.89(3); C21–Pd1–P1, 79.85(10); C21–Pd1–P2, 80.06(10); P1–Pd1–Cl1, 98.74(4); P2–Pd1–Cl1, 101.29(3).

this reaction.[5] In our hands catalyst **2a** gives 50% conversion to 1-phenyl-but-3-en-1-ol, **9**, in THF at 40 °C after 18 hours. In contrast the complex **5b** shows improved performance, giving 78% conversion even at 0 °C in 18 hours. Presumably this increase in activity is a consequence of the increased π-acidity of the P-donors in **5b** compared with **2a**. As well as showing increased activity, complex (*S*)-**5b** gives reasonable enantioselectivity; the product is obtained in 54.5% e.e. (*R*-isomer). A brief solvent optimisation (THF, C_6H_5Me, MeCN, 2-$MeOCH_2CH_2OH$, CH_2Cl_2) revealed CH_2Cl_2 as the solvent of choice and this was used for the rest of the studies.** Under these conditions **10** was obtained in 80% yield and 62% e.e. (*R*). When (*R*)-**5a** is used as the catalyst both the yield of **9** and enantioselectivity suffer (18% and 6% (*S*) respectively). Evidently the *tert*-butyl groups on the resorcinol backbone of **5b** play a significant role in organising the disposition of the binolate residues over the active site of the catalyst and, as anticipated, this leads to higher enantiodiscrimination and also greater catalyst stability.



(1)

The complexes **5c** and **d** both perform poorly (30 and 45% yield respectively, essentially racemic). The non-orthometallated intermediate **8** was also tested and showed essentially identical enantioselectivity as complex **5b** (63% e.e., *R*) but with a significantly reduced conversion of 23%. This may indicate that **8** converts to an active pincer complex *in situ*, however ^{31}P NMR spectroscopy reveals that while a range of P-containing species are formed in the reaction of either 2 or 20 equiv. of allyltributyltin with complex **8**, in the absence of benzaldehyde, under the same conditions as the catalytic reaction, there appears to be no evidence for the formation of a pincer complex.

In summary we have shown that palladium bis(phosphite) *PCP*-pincer complexes can be synthesised *via* C–H bond activation either by: (a) slow thermal reaction which can be vastly accelerated by the use of microwave heating or (b) base-assisted deprotonation. The resultant pincer complexes show both enhanced activity in the allylation of aldehydes compared with bis(phosphinite) *PCP*-pincer complexes and promising enantioselectivity. Research is ongoing into the optimisation of the chiral pincer ligands for maximum activity and enantioselectivity.

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Notes and references

‡ The designators *S* or *R* refer to the stereochemistry of the parent BINOL.
§ See supporting information for synthesis and characterisation of ligands and complexes.
¶ See Fig. S1 in supporting information for the structure of complex **5a**.
‖ **Crystallographic data for complexes. Complex 8:** $C_{108}H_{88}Cl_4O_{12}P_4Pd_2$, M = 2056.26, monoclinic, a = 15.6433(17), b = 19.522(3), c = 18.184(2) Å, β = 93.354(5)°, V = 5543.7(12), T = 100(2) K, space group $P2_1$, Z = 2, μ = 4.484 mm^{-1}, R_{int} = 0.0637 (for 21718 measured reflections), $R1$ = 0.0573 [for 11754 unique reflections with $I > 2\sigma(I)$], $wR2$ = 0.1400 (for all 14271 unique reflections). **Complex 5a:** $C_{49}H_{30}Cl_{10}O_6P_2Pd$, M = 1237.57, monoclinic, a = 10.425(2), b = 9.2502(19), c = 25.909(5) Å, β = 95.57(3)°, V = 2486.8(9), T = 293(2) K, space group $P2_1$, Z = 2, μ = 1.024 mm^{-1}, R_{int} = 0.0579 (for 17578 measured reflections), $R1$ = 0.0666 [for 8341 unique reflections with $I > 2\sigma(I)$], $wR2$ = 0.1381 (for all 10930 unique reflections). **Complex 5b:** $C_{56}H_{45}Cl_7O_6P_2Pd$, M =1230.41, 120 K, orthorhombic, $P2_12_12_1$, a = 9.7215(14), b = 21.165(4), c = 25.864(4) Å, Z= 4, μ = 0.811, reflections measured/obs = 38750/10489, R_{int} = 0.0443, $wR2$ = 0.0861 (all data), R = 0.0380 (obs). CCDC 614135–614137. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b609704a
** Representative method for catalysis: A solution of PhCHO (0.076 ml, 0.75 mmol) and catalyst (5 mol%, added from a stock solution) in CH_2Cl_2 (2 ml) was cooled to 0 °C and stirred for 1 h. $C_3H_5SnBu_3$ (0.280 ml, 0.90 mmol) was added dropwise and the reaction mixture was stirred at 0 °C for 18 h, then sat. $NaHCO_3$(aq) (2 ml) was added, the product was extracted with CH_2Cl_2 (2 × 10 ml), dried ($MgSO_4$) and the solvent was removed gently under reduced pressure without heating. Mesitylene (internal standard, 0.166 M in $CHCl_3$, 1.00 ml) was added, the solvent removed gently and the yield was determined by ^1H NMR spectroscopy ($CDCl_3$). Enantioselectivity was determined by HPLC (Chiralcel OD) and absolute configuration determined by comparison of relative R_f values of both isomers of **10** with literature values.

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