ChemComm

On the effect of catalyst loading in Pd-catalysed allylic alkylation†

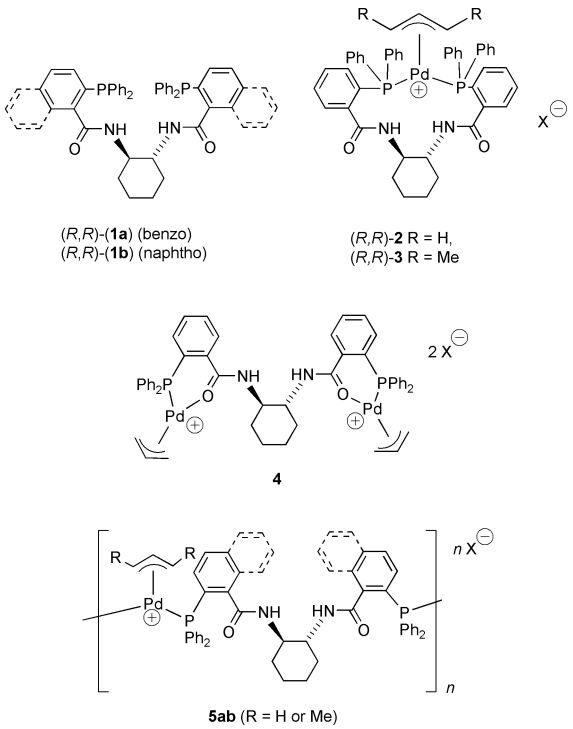
Ian J. S. Fairlamb and Guy C. Lloyd-Jones*

School of Chemistry, Cantock's Close, Bristol, UK BS8 1TS. E-mail: guy.lloyd-jones@bris.ac.uk

Received (in Cambridge, UK) 26th September 2000, Accepted 30th October 2000
First published as an Advance Article on the web 24th November 2000

A mononuclear Pd–allyl complex of the Trost modular ligand displays non-C_2-symmetric ligand coordination and is in equilibrium with a hierarchical series of non-chelate oligomers.

We have an ongoing interest in 'memory effects'[1] in Pd-catalysed allylation, particularly in relation to reactions involving the Trost modular ligand **1a**.[2] During such processes, the coordination mode of **1a** to Pd in Pd–allyl intermediates is generally assumed to be exclusively *P*,*P* chelating and C_2-symmetric[3] (*e.g.*, **2**/**3**). However, the crystalline binuclear complex $[Pd_2(\mathbf{1a})(allyl)_2]^{2+}$, an active catalyst for allylation, is readily prepared.[1b] In the solid state and in solution this exists as a single species **4** (X = OTf) in which Pd is *P*,*O*− coordinated. In stark contrast, the mononuclear species '[Pd(**1a**)(allyl)]$^+$' is an amorphous solid which dissolves to give a number of *P*−coordinated species (^{1}H, ^{13}C and ^{31}P NMR).



A 23 mM solution of '[Pd(**1a**)(allyl)]$^+$' in CD_2Cl_2 at 25 °C displays two distinct sets of ^{31}P NMR signals of approximately equal abundance [Fig. 1(a)]. The first is a cluster of signals in the range δ 24.5–27. These have no discernible coupling and comprise two outer sets of signals and a broader major central set [Fig. 1(a), open square].

The second set is a pair of AB spin systems in a ratio of 62.5 : 37.5 [Fig. 1(a), open/closed circles] the ratio of which varies with temperature [Fig. 1(b)]‡ but not concentration (1–180 mM). The identical $^2J_{PP}$ coupling (32.9 Hz), similar chemical shifts and low entropic difference (ΔS^0 = 2.4 ± 0.1 J K^{-1} mol^{-1}) suggests these to be diastereoisomers. Note that π-allyl rotamers of **2** can only be non-degenerate through non-C_2-symmetric conformation of coordinated ligand **1a**.[3] Above −15 °C, concentration *independent* line-broadening§ indicates unimolecular diastereoisomer interconversion just below the NMR time-scale [*cf.* Fig. 1(a) and (b)].

When the concentration of '[Pd(**1a**)(allyl)]$^+$' is increased, the proportion of **2** decreases [Fig. 1(c)]. Dilution confirms a reversible equilibrium governed by a term or terms of type $[Pd]^n$, where $n > 1$, and thus a monomer-oligomer equilibrium. As predicted, lower temperatures favour oligomer [see Fg. 1(b)], presumably due to substantial ΔS; however, a reliable van't Hoff relationship (−75 → 25 °C) could not be established owing to precipitation at lower temperatures. ^{31}P NMR analysis of the mol fraction **1a** in monomeric *vs*. oligomeric species at varying concentration (1–180 mM, CD_2Cl_2, 25 °C) yields a curve [Fig. 2(a)]. Using sequential equilibria between hierarchical oligomers [*i.e.* $(X)_n$ + **2** ↔ $(X)_{n+1}$, where '*X*' is an unspecified Pd complex] as a model[4] we could successfully predict equilibrium concentrations (solid line). In DMSO-d_6, near-identical diastereomer ratios (63 : 37) and monomer–oligomer concentration dependences were observed.

The monomer–oligomer equilibria does not cause observable ^{31}P NMR line-broadening in **2**, and thus monomer–oligomer

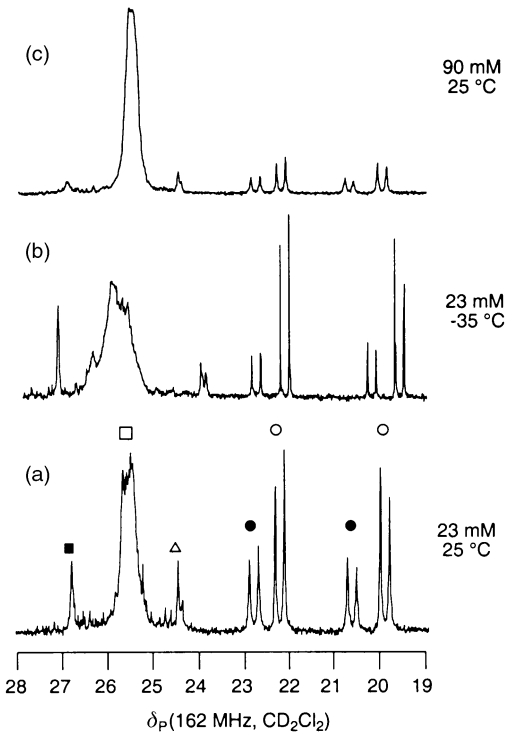


Fig. 1 ^{31}P NMR spectra of [Pd(**1a**)(allyl)][OTf] in CD_2Cl_2 at two temperatures and concentrations. Circles: monomer **2** (R≡H, two diastereomers), open square: oligomer **5a** (R = H), filled square: tentatively assigned as '$[Pd_2(\mathbf{1a})_3(allyl)_2]^{2+}$' (reversibly generated by addition of 0.5 equivalent **1a**), triangle: *P*,*O*-coordinated species analogous to **4** or mono- and *bis*-*P*-allylated **1a** {isochronous with an independently prepared sample of [*P*,*P*′-$allyl_2$-**1a**][$(OTf)_2$]}.

† Electronic supplementary information (ESI) available: explanation of varying ee with catalytic loading. See http://www.rsc.org/suppdata/cc/b0/b007785m/

DOI: 10.1039/b007785m

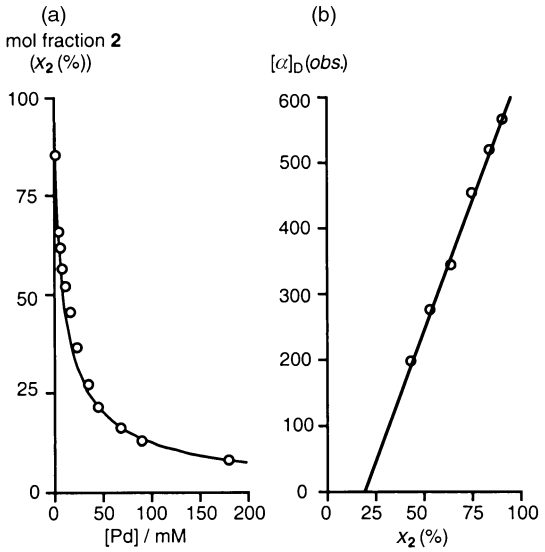
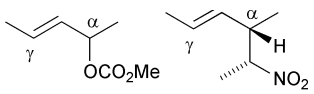


Fig. 2 (a) Concentration of '[Pd(**1a**)(allyl)][OTf]' in CD_2Cl_2 ('[Pd]', *x*-axis) *vs*. mol fraction **2** (x_2, *y*-axis) data: circles (^{31}P NMR) line: best fit. (b) Mol fraction **2** [x_2 (%), *x*-axis] at concentrations of [Pd(**1a**)(allyl)][OTf] in the range 3 → 20 mM *vs*. ($[\alpha]_D$, *y*-axis) circles: data, line: linear regression of $[\alpha]_D$ (obs.) = $[x_2\{\alpha_2\}_D + (100 - x_2)\{\alpha_5\}_D]$.

interconversion is slower than the NMR timescale. However, the specific rotation of [Pd(**1a**)(allyl)][OTf] in CH_2Cl_2 at 22 °C varies dramatically with concentration, *vide infra*, and fast equilibrium ($t_{1/2} \leq 2$ s)[5] at the real time-scale was confirmed by polarimetry after rapid dilution (100 → 10 mM). Analysis of mol fraction monomer (x_2, ^{31}P NMR) and $[\alpha]_D$ over a range of concentrations [Fig. 2(b)] reveals a simple relationship. This demonstrates that the variation of the net specific rotation, $[\alpha]_D$ (obs.), does not arise from large concentration dependent rotations of individual species, but rather from the monomer–oligomer distribution. Linear regression¶ yields an intrinsic specific rotation,[6] $\{\alpha\}_D$ for **2** (R = H) of +644 (±8). The linearity of x_2 *vs*. $[\alpha]_D$ (obs.) also suggests congruence in the $[\alpha]_D$ of the (lower) oligomers and extrapolation to $x_2 = 0$ yields $\{\alpha\}_D = -151$ (±17). This value is significantly different in sign and magnitude from that of **2** and hints that the oligomers are not of the form $(\mathbf{2})_n$. Given the propensity for **1a** to exist in an elongated conformation[1] and the size of the chelate ring in **2** (13-membered) we suggest oligomeric structures of type **5a** (R = H)[7] where the central chirality of the diamide backbone is not within a chelate ring {*cf*. monomer **4** ($[\alpha]_D = 38$, $c = 0.1$, CH_2Cl_2) and ligand **1a** ($[\alpha]_D = 61$, $c = 2.3$, CH_2Cl_2)}.



(±)-**6** (2*R*, 3*S*)-**7**

In recent reports on the asymmetric allylation of $EtNO_2$ by (±)-**6** (→**7**) which is suggested to proceed *via* intermediate π-allyl complex **3**, moderate ee values at high catalyst loadings were suggested to be the result of a memory effect arising through slow interconversion of isomers of **3** of differing symmetry. For example with 4 mol% 'Pd(**1a**)', **7** was obtained in 53% ee whilst with 0.5 mol% the ee increased to 97% ee. It was suggested that 'by lowering the catalyst loading which, in effect, reduces the concentration of the π-allylpalladium intermediate, the unimolecular equilibration event now *outcompetes* the bimolecular nucleophilic addition'.[2a] However, if equilibration is unimolecular and capture by nucleophile is bimolecular, as suggested, then the relative rates of these processes is given by $\{k_{eq}[\mathbf{3}]/k_{Nu}[\mathbf{3}][Nu]\}$. Since this reduces to $\{k'[Nu]^{-1}\}$, in which catalyst loading does not feature, this interpretation of memory effect attenuation‖ is unsatisfactory. However, in view of the results described herein, the possibility of analogous equilibrium between **3** and oligomers** such as **5a** (R=Me) must be considered. In contrast to oligomeric intermediates, *P*,*P*-chelation in **3** will allow efficient central chirality transmission through the helical Ar_3P-donor arrays,[8] albeit in a non-C_2-symmetric fashion.[3] Lower catalyst loadings, favouring monomer, would thus lead to higher selectivity. Furthermore, oligomerisation may also account for decreased selectivities at lower temperatures[3b] or the superiority of **1b** over **1a** (see **5b**)[9] in certain processes.

We thank the EPSRC (GR/N05208) and Lancaster Synthesis for generous support.

Notes and references

‡ A van't Hoff analysis of ^{31}P NMR integrals from spectra obtained between +25 and −75 °C yielded: $\ln K_{eq} = (221 \pm 2.9/T) - 0.283 \pm 0.01$; $r^2 = 0.999$.

§ Line width, $\omega_{1/2}$: 6 ± 1.5 Hz (25 °C, 1–180 mM) → 2 ± 0.5 Hz (constant −15 to −75 °C). Strong correlations between A/B′ and A′/B and weak correlations between A/A′ and B/B′ in the 2D ^{31}P{^{1}H} EXSY (500 MHz) spectrum [δ_P, 22.2/19.9 (A,B) and 22.8/20.6 (A′,B′)] suggest that equilibrium proceeds *via* interconversion of ligand conformation rather than ligand dissociation, or π–σ–π allyl fluxionality.

¶ The principle of optical superposition (van't Hoff) is assumed to apply.

‖ The lower selectivity at higher catalyst loading (4 mol%) does not arise exclusively from a regiochemical memory effect (see Fig. 3 in ESI†).

** Ionisation of **6** may generate **3** directly, or indirectly *via* oligomeric Pd(0) species.

1 (*a*) G. C. Lloyd-Jones and S. C. Stephen, *Chem. Eur. J.*, 1998, **4**, 2539 and references therein; (*b*) C. P. Butts, J. Crosby, G. C. Lloyd-Jones and S. C. Stephen, *Chem. Commun.*, 1999, 1707; (*c*) A. J. Blacker, M. L. Clarke, M. S. Loft and J. M. J. Williams, *Org. Lett.*, 1999, **1**, 1969; (*d*) G. C. Lloyd-Jones, S. C. Stephen, M. Murray, C. P. Butts and Š. Vyskočil and P. Kočovský, *Chem. Eur. J.*, 2000, **6**, 4348; (*e*) J. M. Longmire, B. Wang and X. Zhang, *Tetrahedron Lett.*, 2000, **41**, 5435; (*f*) B. Goldfuss and U. Kazmaier, *Tetrahedron*, 2000, **56**, 2493.

2 (*a*) B. M. Trost and J.-P. Surivet, *J. Am. Chem. Soc.*, 2000, **122**, 6291; (*b*) B. M. Trost and J.-P. Surivet, *Angew. Chem., Int. Ed.*, 2000, **39**, 3122.

3 As far as we are aware, there is no published experimental data on the symmetry of *P*,*P*-chelate coordination of **1a** to Pd. However, the working model, based on molecular modelling, always employs fully C_2-symmetric coordination: (*a*) B. M. Trost and F. D. Toste, *J. Am. Chem. Soc.*, 1999, **121**, 4545; however, also see footnote 36 in (*b*) B. M. Trost and X. Ariza, *J. Am. Chem. Soc*, 1999, **121**, 10 727.

4 Quantitative analysis of monomer-oligomer equilibrium will be described elsewhere.

5 Slow equilibration is observed in $PdCl_2$ complexes of simple (achiral) diphosphines with alkyl or polyether backbones: D. C. Smith and G. M. Gray, *J. Chem. Soc., Dalton Trans.*, 2000, 677; however, the ability of **1a** to act as a *P*,*O*-donor to cationic Pd(II) (as in **4**) may catalyse interconversion.

6 There are no observable chromophores in the region of the sodium D-line in the UV spectrum of the mixture of complexes: E. L. Eliel and S. H. Wilen, *Stereochemistry of Organic Compounds*, John Wiley and Sons, New York, 1994.

7 Such oligomers could be linear or cyclic, see *e.g.* B. L. Shaw, *J. Organometal. Chem.*, 1980, **200**, 307.

8 The major contributor to the magnitude and sign of the optical rotation is likely to be the degree of order and sense of the aryl phosphine rotors. The sextuple phenyl array is the mainstay of the 'cartoon' representation of the 'chiral pocket'. Since ligand **1a** is particularly effective with slim cyclic allyl substrates and less so with bulky linear ones (see *e.g.* B. M. Trost, A. C. Krueger, R. C. Bunt and J. Zambrano, *J. Am. Chem. Soc.*, 1996, **118**, 6520) the tightness of the 'chiral pocket' may exacerbate oligomerisation with the latter class.

9 B. M. Trost, R. C. Bunt, R. C. Lemoine and T. L. Calkins, *J. Am. Chem. Soc.*, 2000, **122**, 5968.