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Phosphine-alkene ligand-mediated alkyl-alkyl and alkyl-halide elimination processes from palladium(II)†

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N-Diphenylphosphino-7-*aza*-benzobicyclo[2.2.1]hept-2-ene (**2**) behaves as a chelating phosphine-alkene ligand for Pd⁰ and Pd^{II}, promoting direct alkyl-alkyl and indirect alkyl-halide reductive elimination due to the stabilisation of the resulting bis(phosphine-alkene)Pd⁰ complex.

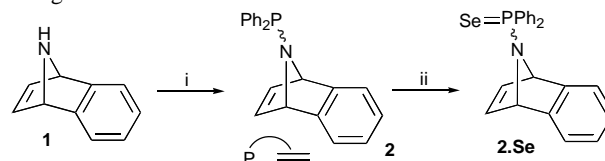
Palladium-mediated catalytic transformations are at the heart of contemporary synthetic organic chemistry, particularly for the controlled formation of C–C and C–heteroatom bonds.^{1,2}

Manipulation of these reactions necessitates a detailed understanding of the overall reaction trajectory and of the individual steps involved in the catalytic cycle. In particular, establishing factors that control reductive elimination from palladium is a key objective, since it is often through this step that final product formation occurs, *via* either a direct (four-coordinate) or indirect (three-coordinate) transition state.^{3,4} The rate of reductive elimination is intimately linked to the nature of the coupling partners and to the palladium's ancillary ligands, with both steric and electronic factors playing a significant contribution in each case.⁵ Significant effort has been devoted to studying the impact of a wide variety of ubiquitous monodentate phosphine and bidentate diphosphine metal scaffolds, with both their σ -donor character and chelate bite angle having been found to impact directly on elimination rates.^{6,7,8,9}

Recently, efforts have begun to focus on the use of heteroditopic chelate ligands to increase control and further promote elimination. For example, a phosphine bearing a pendant electron deficient alkene has been shown to favour reductive elimination over a competing β -hydride elimination reaction pathway in Negishi cross-couplings.^{10,11} The system's selectivity was attributed to the presence of the strongly π -accepting alkene moiety.

Since it is now well established that weakly *trans* influencing, poorly-donating/electron-accepting phosphines favour reductive elimination from Pd^{II}, we sought to explore the efficacy of a chelating phosphine-alkene (P-alkene) framework combining a weakly basic R₃P moiety with a strongly π -accepting alkene unit.^{12,13,14} To this end, we describe here our use of a strained bicyclic 7-*aza*-norbornene motif to maximise Pd-to-alkene π -retrodonation through relief

of ring strain.

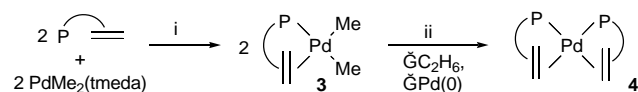


Scheme 1 Conditions: i) Ph₂PCl, NEt₃, CH₂Cl₂, –30 °C to r.t., 12 h, 69%; ii) Se, CDCl₃, r.t., 15 mins., 100%.

The ligand *N*-Ph₂P-7-*aza*-benzobicyclo[2.2.1]hept-2-ene (**2**) was prepared in 69% yield from 7-*aza*-benzobicyclo[2.2.1]hept-2-ene (**1**), *via* a straightforward nucleophilic substitution strategy, Scheme 1.^{15,16,†} Compound **2** presents a single resonance by ³¹P{¹H} NMR spectroscopy, $\delta^{31}\text{P}\{\text{H}\}$ 41.6 ppm, typical of an aminophosphine.¹⁷ The barrier to inversion at nitrogen in compound **2** has been determined computationally (B3LYP/6-31G*) to be low, ~3 kcal mol⁻¹ (*cf.* 16 kcal mol⁻¹ computed for amine **1**), permitting **2** to adopt the necessary conformation for κ^2 -P,C P-alkene metal chelation. The magnitude of ¹J_{Se-P} (792 Hz) for the phosphine-selenide **2·Se** confirms that the phosphorus donor moiety of **2** is weakly basic.^{17,†}

To probe the ability of P-alkene **2** to enhance reductive elimination from Pd^{II}, its reaction with PdMe₂ and PdCl(Me) fragments has been explored. Treating a toluene solution of PdMe₂(tmeda) with one equivalent of compound **2** cleanly affords *cis*-[PdMe₂(κ^2 -P,C-**2**)] (**3**), which exhibits a single resonance ($\delta^{31}\text{P}\{\text{H}\}$ 81.2 ppm), consistent with P-Pd binding. Coordination of the olefinic moiety is reflected in a shift to lower frequency of the alkene carbon resonance (**2**: δ 144.3 ppm; **3**: δ 119.2 ppm).

Complex **3** is thermally unstable in solution and over 5 days at r.t. smoothly evolves to afford half an equivalent of the monometallic Pd⁰ complex [Pd(κ^2 -P,C-**2**)] (**4**) ($\delta^{31}\text{P}\{\text{H}\}$ +82.3 ppm) and ethane ($\delta^1\text{H}$ 0.82 (s) ppm) as the only organic product, according to ¹H and ³¹P NMR spectroscopy, accompanied by the precipitation of elemental palladium (Scheme 2).§ By comparison, complete thermolysis of [PdMe₂(dmpe)] is only achieved upon heating at 90 °C for 1 week,^{18,19} highlighting the potential of ligand **2** in promoting reductive elimination processes.

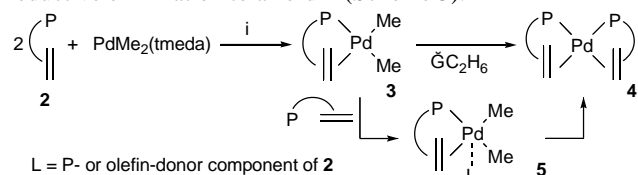


Scheme 2 Conditions: i) toluene, r.t., >99%; ii) toluene, r.t., 120 h, >99%.

The X-ray molecular structures of complexes **3** and **4** (Fig. 1)† confirm κ^2 -P,C chelation of **2**. In complex **3** the palladium centre is planar, with one site occupied by the midpoint (Md) of the η^2 -bound C(2)=C(3) bond, which is inclined by 88.3° to the coordination plane. The bond distances to palladium fall within the range observed for other complexes of the type *cis*-[PdCl₂(η^2 -C=C)(PR₃)].^{20,21,22,23,24} Consistent with moderate Pd→ $\pi^*(\text{C}=\text{C})$ retro-donation, the C(2)=C(3) bond in **3** (1.359(3) Å) is longer than the corresponding bond in an uncoordinated analogue of **2**, *N*-BOC-*aza*-benzonorbornadiene oxadisilole (1.315(4) Å).²⁵

In complex **4**, the Pd coordination geometry is distorted-tetrahedral, with the Md-Pd-P planes of the two P-alkene ligands forming an 89.1° dihedral angle. Although the η^2 -coordinated C=C bonds of **4** are longer (1.401(2) and 1.406(2) Å) than that of **3**, as would be expected, the difference is only moderate due to the comparatively poor π -donor character of d¹⁰ palladium species.²⁶

If PdMe₂(tmeda) is treated instead with **2** in a Pd:2 ratio of 1:2, much faster and quantitative formation of **4** is achieved (5 h, 20 °C) consistent with rapid reductive elimination. Investigation of this reaction by variable temperature NMR spectroscopy (VT NMR) did not reveal any intermediates on the pathway from **3** to **4**. Consequently, we propose that the second equivalent of ligand **2** reacts with complex **3** to form a five-coordinate intermediate **5**, which then undergoes rapid reductive elimination to afford **4** (Scheme 3).



Scheme 3 Conditions: i) toluene, r.t., >99%.

The rate of reductive elimination from complex **5** is likely to be much greater than that from tetracoordinate complex **3** since prior reports have clearly established rate enhancements in reductive elimination with increasing coordination number.²⁷ The intermediacy of a five-coordinate species here is further supported by the observation that treating complex **3** with either 5 mol% of PPh₃ or propene both lead to a significant increase in the rate of reductive elimination of ethane, with formation of **4** being complete within 7 and 30 h, respectively, at 20 °C (*cf.* 120 h in the absence of L-donor ligand).

To probe the role of the alkene moiety of **2** in promoting reductive elimination from **3**, the P-alkane ligand **6** ($\delta^{31}\text{P}\{^1\text{H}\}$ 38.6 ppm), possessing an *aza*-norbornane rather than *aza*-norbornene framework, was prepared from *N*-BOC-7-*aza*-benzobicyclo[2.2.1]heptane.^{28,†} Reaction of two equivalents of **6** with PdMe₂(tmeda) in toluene forms *cis*-[PdMe₂(κ^1 -P-**6**)₂] (**7**), $\delta^{31}\text{P}\{^1\text{H}\}$ 61.0 ppm, which cleanly isomerises to the *trans*-diphosphine complex **8** ($\delta^{31}\text{P}\{^1\text{H}\}$ 59.7 ppm,) over a period of 24 h at 20 °C (Scheme 4); no further reaction of **8** is

observed even in the presence of excess **6** at 60 °C. Clearly κ^2 -P,C chelation is vital in retaining the necessary *cis* geometry for reductive elimination from **3**.

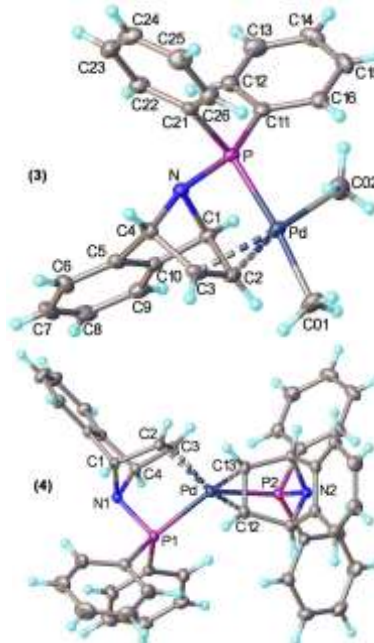
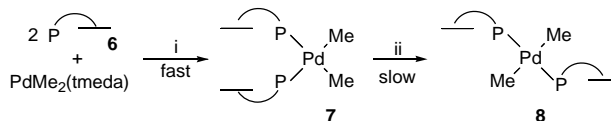
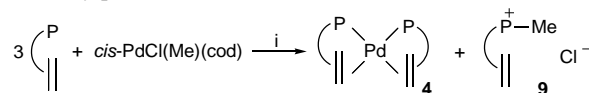


Fig. 1 X-ray molecular structures of **3** and **4**; thermal ellipsoids at 50% probability level. Selected bond distances (Å) in **3**: Pd–P 2.2876(6), Pd–C(01) 2.068(3), Pd–C(02) 2.074(3), Pd...C(2) 2.238(2), Pd...C(3) 2.266(2), P–N 1.732(2); in **4**: Pd–P(1) 2.3440(4), Pd–P(2) 2.3341(4), Pd...C(2) 2.1901(14), Pd...C(3) 2.1912(15), Pd...C(12) 2.2095(15), Pd...C(13) 2.1916(14), P(1)–N(1) 1.7470(13), P(2)–N(2) 1.7454(13).



Scheme 4 Conditions: i) toluene, r.t., >99%; ii) toluene, r.t., 24 h, >99%.

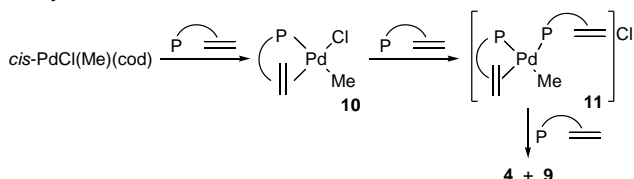
Due to significant M–Cl bond polarisation the barrier to alkyl chloride reductive elimination is much greater than that for alkyl-alkyl elimination; consequently, to the best of our knowledge no examples from Pd^{II} have been reported.¹⁴ Therefore we were interested to probe whether P-alkene ligand **2** could also promote alkyl halide elimination. Notably, reaction of **2** with *cis*-PdCl(Me)(cod) (Pd:2 = 1:1) does indeed give rise to Pd⁰ complex **4** (consistent with reductive elimination), which is formed extremely rapidly (reaction complete within seconds at –40 °C according to VT NMR). However, **4** is obtained along with an equimolar quantity of **9** ($\delta^{31}\text{P}\{^1\text{H}\}$ 38.1 ppm), the methyl phosphonium chloride salt of **2**, and leaving unreacted palladium starting material. In contrast, treating *cis*-PdCl(Me)(cod) with three equivalents of **2** rapidly and quantitatively affords a 1:1 mixture of **4** and **9** as the only products (Scheme 5).



Scheme 5 Conditions: i) toluene, r.t., >99%.

An analogous reaction of *cis*-PdCl(Me)(cod) with two or three

equivalents of the P-alkane ligand **6** (~5 mins, 20 °C) affords only *trans*-[PdCl(Me)(κ¹-P-**6**)₂] (**10**) (δ ³¹P 6.7 ppm). To account for the formation of **4** and **9** it is proposed that initially [PdCl(Me)(κ²-P,C-**2**)] (**10**) is formed, which undergoes rapid chloride ligand substitution (labilised by the *trans* alkene moiety²⁹) by **2** to form complex **11**. In the presence of free ligand **2**, complex **11** then undergoes *pseudo*-reductive elimination affording phosphonium salt **9** and Pd⁰ complex **4** (Scheme 6). Presumably, methyl-to-phosphorus migration is favoured here by the electron deficient nature of the amido-substituted phosphorus centre. Access to a pathway along which phosphonium salts may be generated is consistent with the formation of Ph₄PI having been observed following Heck coupling reactions involving [PdI(Ph)(PPh₃)₂] precatalysts.³⁰



Scheme 6 Proposed pathway for the formation of phosphonium salt **9**.

In conclusion, by combining a readily prepared, poorly-donating phosphine component with a strongly π-accepting alkene moiety in a single bidentate ligand framework, **2**, it has been possible to efficiently promote reductive elimination from Pd^{II} complexes. The effectiveness of ligand **2** is attributed, in part, to its ability to form a stable *bis*(phosphine-alkene)Pd⁰ complex, **4**, together with its *cis*-bidentate coordination. Notably, the inclusion of an electron poor phosphine moiety can also allow access to less common intramolecular *pseudo*-reductive elimination processes involving the coordinated phosphorus centre, resulting in phosphonium salt formation, in what can be regarded as a rare example of reductive elimination of chloromethane from Pd^{II}. Work is on-going to probe the utility of ligands such as **2** in a variety of catalytic applications.

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Notes and references

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† Electronic supplementary information (ESI) available: experimental details and characterization data, including crystallographic data for **3** and **4**; computational studies. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/abcdefg

§ Integration of both the ¹H and ³¹P[¹H] NMR spectra was quantified using an internal standard.

‡ Bruker SMART 6000 CCD area detector, Mo-K_α radiation (λ=0.71073 Å), T=120 K, Olex2 software.³¹ Crystal data: **3**, C₂₄H₂₄NPPd, M= 463.81,

55 monoclinic, space group P2₁/c (no. 14), a= 10.2185(3), b= 10.6113(4), c= 19.2717(7) Å, β=104.176(14)°, U= 2026.0(1) Å³, Z=4, μ=1.00 mm⁻¹, 26057 reflections (2θ≤60°), R_{int}=0.061, R=0.031 on 4196 data with I≥2σ(I), wR(F²)=0.061 on all 5912 unique data. CCDC 894607. **4**, C₄₄H₃₆N₃P₂Pd, M= 761.09, triclinic, space group P-1 (No. 2), a=11.9327(6), b=12.2787(6), c=13.2937(6) Å, α=70.057(7), β=74.120(7), γ=81.517(7)°, U=1757.92(7) Å³, Z=2, μ=0.65 mm⁻¹, 40908 reflections (2θ≤70°), R_{int}=0.038, R=0.036 on 11656 data with I≥2σ(I), wR(F²)=0.088 on all 14631 unique data. CCDC 894608.

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