Platinum-mediated aryl–aryl bond formation and sp^3 C–H bond activation†

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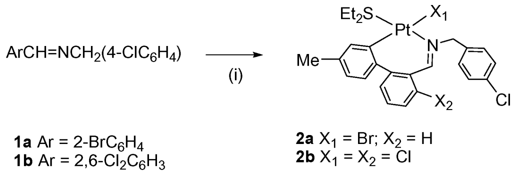
Received 23rd April 2010, Accepted 15th June 2010
First published as an Advance Article on the web 23rd June 2010
DOI: 10.1039/c0dt00631a

A novel process is described in which intramolecular oxidative addition is followed by aryl–aryl bond formation and sp^3 C–H bond activation leading to a six-membered platinacycle.

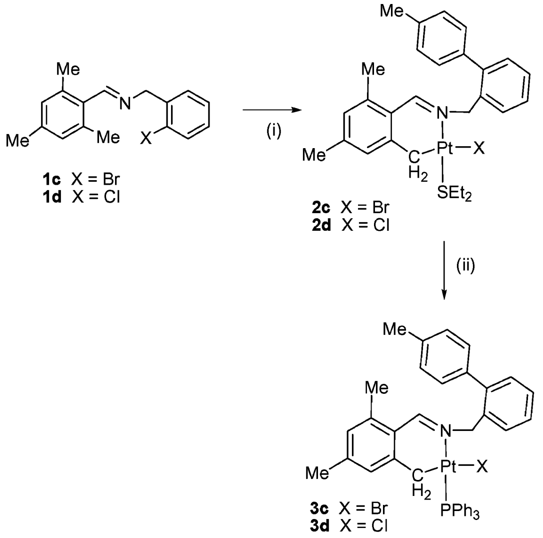
The biaryl motif is a predominant feature in many pharmaceuticals and bioactive compounds. For this reason, the development of new methods for aryl–aryl bond formation, often involving transition-metal-mediated reactions, is a field of great interest.[1]

We have recently reported a process involving C–C coupling and formation of seven-membered platinum(II) metallacycles in the reactions of *cis*-[Pt$_2$(4-MeC$_6$H$_4$)$_4$(μ-SEt$_2$)$_2$] with ligands ArCH=NCH$_2$(4-ClC$_6$H$_4$) (Ar = 2-BrC$_6$H$_4$ (**1a**); 2,6-Cl$_2$C$_6$H$_3$ (**1b**) shown in Scheme 1) or with the corresponding potentially terdentate ligands ArCH=NCH$_2$CH$_2$NMe$_2$. It has been shown that these reactions take place through initial intramolecular C–X (X = Br or Cl) bond activation to produce a cyclometallated platinum(IV) compound.[2] In this case, as well as in related C–C coupling processes leading to either seven-[3] or five-membered[4] platinacycles, the activation of the C–X bond gives a metallacycle containing the imine functionality (*endo*-metallacycle) and the C–C coupling takes place between a freely rotating aryl group and a rigid aryl ring of a metallacycle.



(i) + [Pt$_2$(4-MeC$_6$H$_4$)$_4$(μ-SEt$_2$)$_2$] in toluene

Scheme 1 Formation of seven-membered platinacycles (Ref. 2).



(i): + [Pt$_2$(4-MeC$_6$H$_4$)$_4$(μ-SEt$_2$)$_2$] in toluene; (ii): + PPh$_3$ in acetone.

Scheme 2 Synthetic method.

In order to progress in understanding the factors that govern these processes, we envisaged analogous reactions with imines such as 2,4,6-C$_6$H$_2$(CH$_3$)$_3$CH=NCH$_2$(2-BrC$_6$H$_4$) (**1c**) for which C–Br bond activation should lead to more flexible *exo*-platinacycles. The mesityl group was chosen in order to block the *ortho* positions of the benzylidene group and drive the reaction towards the benzyl ring of the ligand. As shown in Scheme 2, C–C bond formation does indeed take place between the benzyl group of the imine ligand and one of the *para*-tolyl groups leading to a biaryl linkage. However, in contrast to previous results, the subsequent C–H activation does not take place at the biaryl system to yield either seven or five-membered metallacycles but instead an aliphatic C–H bond of the mesityl group is activated to produce a six-membered *endo*-metallacycle (compound **2c**). Due to the low stability of **2c**, the triphenylphosphine derivative **3c** was also prepared and fully characterised.[5] Crystals of **3c** just good enough for structure resolution were obtained and allow for definitive confirmation of the formation of an aryl–aryl bond and of a six-membered platinacycle (Fig. 1).[6] The resulting biaryl linkage is pointing away from the platinum centre and the two phenyl rings are tilted 66.3(4)° from each other.

Ligand 2,4,6-C$_6$H$_2$(CH$_3$)$_3$CH=NCH$_2$(2-ClC$_6$H$_4$) (**1d**) was also tested and produced an analogous reaction to that reported for **1c** while ligand 2,4,6-C$_6$H$_2$(CH$_3$)$_3$CH=NCH$_2$C$_6$H$_5$ (**1e**) failed to react. These results indicate that C–X bond activation (X = Br or Cl) to produce a platinum(IV) metallacycle is required for the process to take place. On the other hand, formation of a six-membered platinacycle through sp^3 C–H bond activation is remarkable since a strong tendency to form five- *versus* six-membered rings as well as a preference for the activation of sp^2 over sp^3 C–H bonds are generally observed in cyclometallation reactions.[7] In particular, platinacycles formed through aliphatic C–H bond activation are uncommon.[8] While activation of a methyl C–H bond of a mesityl group with formation of six membered

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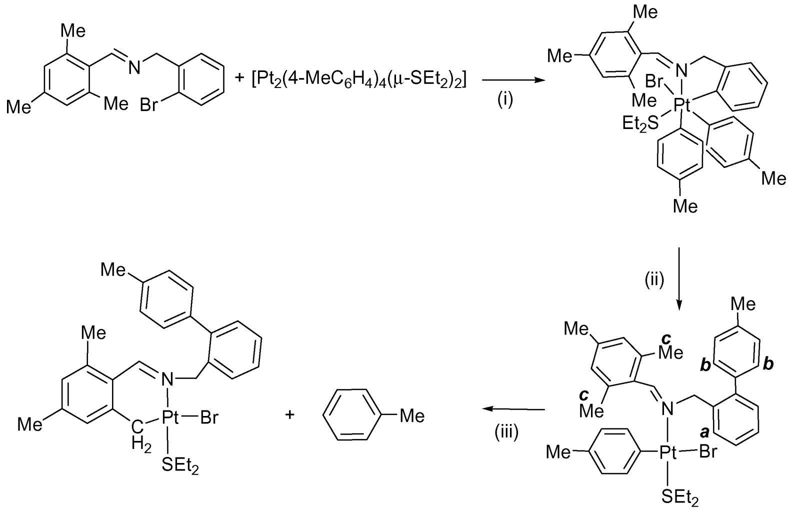
† Electronic supplementary information (ESI) available: Experimental procedures and characterization data for all new compounds. CCDC reference number 774868. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c0dt00631a



(i): Intramolecular C-Br bond activation; (ii): Reductive elimination with formation of an aryl-aryl bond; (iii): Cyclometallation at the methyl group.

Scheme 3 Proposed reaction pathway.

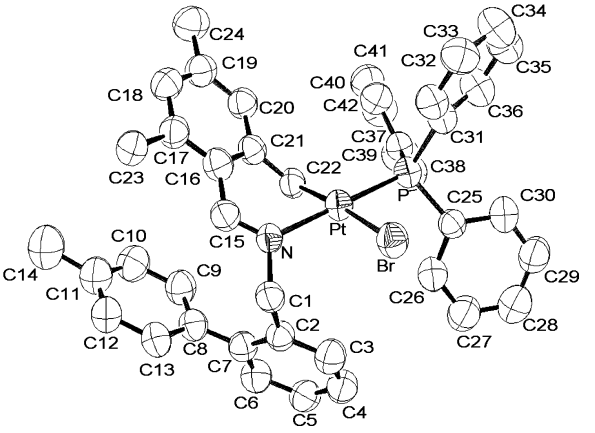


Fig. 1 Molecular structure of compound **3c** showing 50% probability ellipsoids.

metallacycles is well known at palladium,[9] such process has not been observed in the reactions of imines **1d** or **1e** with platinum substrates *cis*-[PtCl$_2$(dmso)$_2$][10] or *cis*-[PtMe$_2$(μ-SMe$_2$)]$_2$[11] which gave instead *exo*-metallacycles through activation of aromatic C–H or C–Cl bonds.

As a whole, the results here reported indicate that intramolecular C–X (X = Br or Cl) bond activation at the saturated arm of the benzylidene-benzylamines may promote, upon reaction with *cis*-[Pt$_2$(4-MeC$_6$H$_4$)$_4$(μ-SEt$_2$)$_2$], the formation of a biaryl linkage between one of the tolyl groups and the benzyl group of the ligand. In contrast to previously reported reactions, the biaryl linkage is not involved in the subsequent metallation which leads to an unusual six-membered platinacycle. These results suggest that the C–C coupling and the cyclometallation are independent steps of the process and allow us to propose the reaction path shown in Scheme 3. In this process, the initial C–X bond activation to produce a platinum(IV) derivative is followed by reductive elimination with formation of an aryl–aryl bond. The final cyclometallation step could lead to either *exo*-five- or *exo*-seven-membered platinacycles through aromatic C–H bond activation (at positions indicated in Scheme 3 as ***a*** and ***b***, respectively) or to an *endo*-six-membered platinacycle arising from aliphatic C–H bond activation (indicated as ***c***). The results here reported reveal that the latter option is the most favoured and this can be related to the higher stability of the *endo versus exo*-metallacycles (the so-called *endo* effect)[7,9] which allows to overcoming the low tendency to form six-membered rings and to activate a sp^3 C–H bond.

In summary, we have succeeded in achieving platinum-mediated C–C coupling using a different type of imine ligand. Moreover, in spite of the fact that the imine functionality is not required for aryl–aryl bond formation, it is decisive for the regioselectivity of the cyclometallation step. Further work aimed at a better understanding and at expanding the scope of the process is currently in progress.

Acknowledgements

We thank the Ministerio de Ciencia y Tecnología (project CTQ2009-11501) for financial support.

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5 Experimental procedures and characterization data for all the new compounds here reported are given in the ESI.† For **3c**, in the methyl region of the ^{1}H NMR spectrum, in addition to the methyl resonance corresponding to the *para*-tolyl group (2.35 ppm), only two resonances integrating 3 hydrogen atoms (1.92 and 2.02 ppm) corresponding to

the mesityl group are observed. The resonance assigned to Pt–CH_2 is observed at 2.06 ppm (J(H–Pt) = 96 Hz) in the ^{1}H NMR spectrum and at 14.70 ppm (J(C–Pt) = 630 Hz) in the ^{13}C NMR spectrum in good agreement with previously reported data for analogous compounds.[8] The large J(P–Pt) value observed in the ^{31}P and ^{195}Pt spectra indicates that the phosphine is *trans* to N rather than to C atom.

6 Compound **3c** crystallized as an hydrate and the water molecule displays positional disorder. $C_{42}H_{39}BrNPPt{\cdot}H_2O$, MW = 881.73, triclinic, space group $P\bar{1}$, $a = 12.032(5)$ Å, $b = 12.230(4)$ Å, $c = 12.715(3)$ Å, $\alpha = 81.08\ (2)°$, $\beta = 72.52\ (2)°$, $\gamma = 79.01\ (2)°$, $V = 1742.3(10)$ Å^3, $Z = 2$, number of reflections collected/unique = 16 366/8758 [R(int) = 0.0627], final R indices [$I > 2\sigma(I)$] $R_1 = 0.0550$, wR_2 = 0.1579, R indices (all data) $R_1 = 0.0551$, wR_2 = 0.1579, GOF = 1.087.

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