Facile intramolecular C(sp^3)–H bond activation with Pd^{II}†

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The treatment of bis(4-*tert*-butylthiazolyl)isoindoline (4-*t*Bu-BTI) with palladium acetate results in the exclusive formation of an organometallic Pd^{II} compound with C–H activated *t*-butyl group and a hemilabile S-coordinated thiazole donor in *cis*-position.

Divalent palladium is known to activate C(sp^2)–H and C(sp^3)–H bonds in intramolecular cyclopalladation reactions.[1] While for C(sp^2)–H and benzylic and allylic C(sp^3)–H activation a significant number of examples exists, non-activated C(sp^3)–H activation by divalent palladium is a rather rarely observed process and usually requires harsh reaction conditions.[2] The best investigated examples so far are the reactions of palladiumacetate with 6-*tert*-butyl-2,2′-bipyridine and related ligands.[3] More recently, auxiliary directed intramolecular Pd^{II} induced C(sp^3)–H activation processes have been proposed to play a vital role in alkyl group activation and catalytic C–C coupling reactions.[4]

In the last years we and others have observed strain-induced and Lewis acid-triggered cyclopalladation reactions of bis(pyridylimino)isoindoline ligands (Fig. 1).[5] While **1** forms as a thermally stable product from L and excess Pd(OAc)$_2$, **2** is the only isolated compound if 4,6-MeBPI is used instead. The reaction proceeds *via* a strained Werner-type complex structurally analogous to **1**, which inverts one of the pyridine side arms in the presence of a second equivalent of palladium acetate. The result tempted us to investigate sterically encumbered ligands of this class with side arms other than pyridine. The use of a thiazole derivative with methyl groups at positions equivalent to those in **2** led to the Werner-type compound only.[6] If these methyl groups are exchanged for *tert*-butyl substituents, however, the reaction takes a different course, and a new compound with C(sp^3)–H activated *tert*-butyl group and S-coordinated thiazole donor in *cis*-position **4** is isolated as a brilliant red solid in 78% yield (Scheme 1). The reaction was carried out using three equivalents of palladium acetate and proceeds smoothly in a range of different solvents (acetonitrile, toluene, methanol, dichloromethane *etc.*) at ambient temperature without any detected side products.

The cyclopalladated molecular structure of **4** is apparent from the proton NMR spectra by the observation of singlets at 2.14, 1.35 and 1.40 ppm with relative intensities of 2 : 6 : 9, that originate from one CH_2, two chemically equivalent CH_3 and one intact *tert*-butyl group, respectively, as well as from the loss of an effective C_2 symmetry. The very unusual S-coordination of the palladium ion is indicated by ^{1}H-NOESY experiments by the observation of cross peaks between the CH_2 group signal and the thiazole proton of the juxtaposed heterocyclic subunit. For a detailed understanding of **4** a single crystal X-ray structural analysis was performed. A suitable single crystal was grown by slow diffusion of *n*-hexane into a solution of **4** in a chloroform–hexafluorobenzene mixture at ambient temperature. The result shows the first crystallographically determined palladium(II) complex with a S-bonded thiazole donor[7] and is shown in Fig. 2.

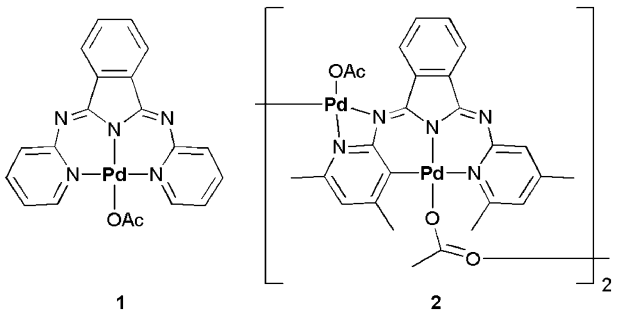
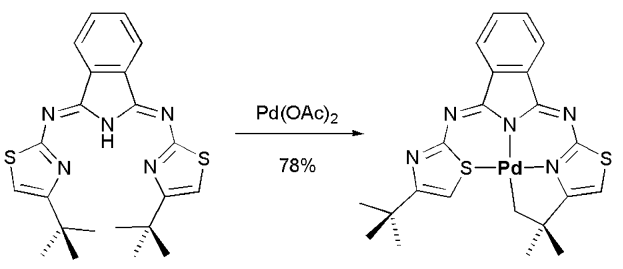


Fig. 1 Werner-type mono- and C–H activated tetranuclear palladium(II) complexes from bis(pyridylimino)isoindoline ligands of different steric encumbrance.

Due to the strong *trans* influence of the carbon donor C1 the Pd–N3 bond in **4** appears elongated to 2.076 Å[8] while on the other hand the Pd–N1 bond is quite short as a consequence of the presence of the restraint by the five-membered ring C, N chelate. The same restraint leads to the pronounced deviation of the N3–Pd–C1 angle from linearity. This deviation is mainly due to an *in-plane* distortion and leaves the PdCN$_2$S coordination unit in the expected planar conformation.

A remarkable feature of **4** is found in the S-coordination of the palladium atom by one of the thiazole subunits. The distance Pd1–S2 of 2.2599 Å appears rather long, but is similar



Scheme 1 Formation of the C(sp^3)–H activated palladacycle **4** from **3**.

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† Electronic supplementary information (ESI) available: Full experimental descriptions, spectroscopic data for **3**, **4** and **5** and crystallographic data in CIF or other format, CCDC 677873 & 677874. See DOI: 10.1039/b802185f

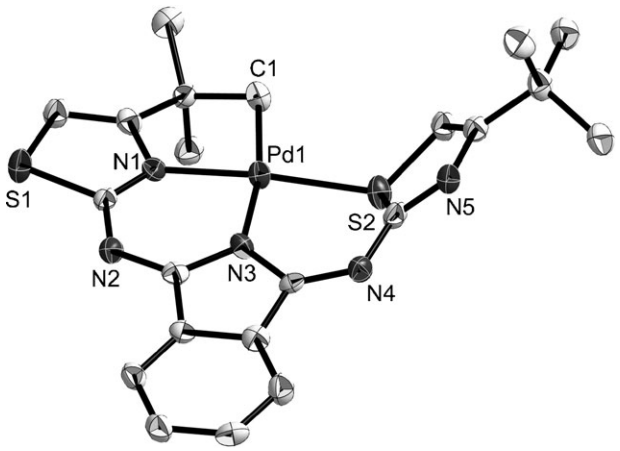

Fig. 2 Molecular structure of **4**. Selected bond lengths (Å) and angles (°): Pd1–N1 1.986(4), Pd1–N3 2.076(4), Pd1–S2 2.2599(13), Pd1–C1 2.037(5); N1–Pd1–N3 88.36(15), N1–Pd1–S2 173.47(11), N1–Pd1–C1 82.34(18), N3–Pd1–S2 91.40(11), N3–Pd1–C1 169.22(18), S2–Pd1–C1 98.46(14). Ellipsoids are set at 50% probability.

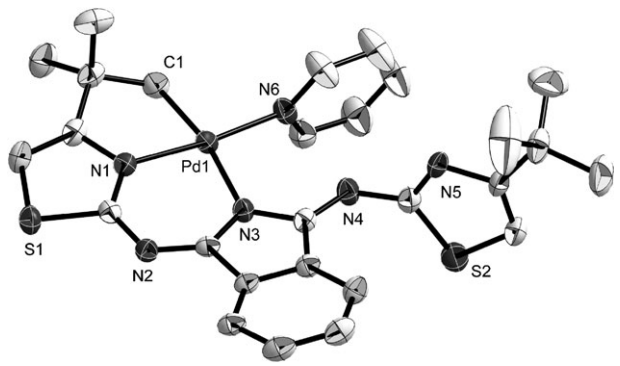

Fig. 3 Molecular structure of **5**. Selected bond lengths (Å) and angles (°): Pd1–N1 1.973(2), Pd1–N3 2.132(2), Pd1–N6 2.047(2), Pd1–C1 2.022(3); N1–Pd1–N3 86.52(8), N1–Pd1–N6 172.11(8), N1–Pd1–C1 82.58(9), N3–Pd1–N6 101.32(8), N3–Pd1–C1 168.78(9), N6–Pd1–C1 89.55(9). Ellipsoids are set at 50% probability.

to the only comparable value found in literature for a related thiophene-based S, N, N chelate[8a] of 2.257 Å. The S-bonded thiazole ring orientation is not coplanar with the $PdCN_2S$ coordination unit but bent from this plane by a dihedral angle of 46.54(6)°. This structural finding points to a weakly bonded and hemilabile S donor that should be easily exchanged by external ligands or solvent molecules. Pyridine was employed in order to prove this hypothesis, and an NMR titration experiment showed that a new compound appears immediately upon the addition of pyridine to a chloroform solution of **4**. This new compound **5** is present as the only species after the addition of 30 equivalents of pyridine. Crystallization from pyridine–*n*-hexane leads to the formation of well-developed red cubes of this newly formed compound **5**. Fig. 3 shows the result of a crystallographic analysis. The molecular structure and conformation found for **5** in the solid state is in agreement with the interpretation of 2D NMR spectra taken in solution (see ESI†).

5 contains the intact $PdCN_2$ fragment of the coordination unit of **4** and presents the thiazole ring uncoordinated and tilted away from the metal ion. A N-bound pyridine donor now occupies the fourth coordination site at the palladium atom in a distance of 2.047 Å. Due to the steric repulsion between the pyridine and the dangling thiazole (the N4···N6 distance of 2.956(3) Å is shorter than the sum of the van der Waals radii of 3.1 Å) the Pd–N3 bond is now elongated to 2.132 Å, and the angles N3–Pd–N6 and N6–Pd–C1 are respectively about 10° larger and smaller in **5** than the equivalent angles N3–Pd–S2 and S2–Pd–C1 in **4**. The Pd–C1 bond, however, appears robust and remains untouched in the transformation.

The results presented here show that a suitable molecular design allows the observation (and presumably the use) of a selective intramolecular $C(sp^3)$–H activation process with acetato palladium derivatives already at ambient temperature. In this case a new complex has been found by this strategy containing a hemilabile donor *cis* to the organometallic Pd–C bond. This complex **4** is ideally suited for reactivity studies and for the visualization of proposed reaction intermediates in modern palladium catalyzed transformations. Work towards these goals is currently under way.

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