

## Palladium-catalysed Regioselective Cyclisation of Unsaturated Bromoanilinoalkenenitriles

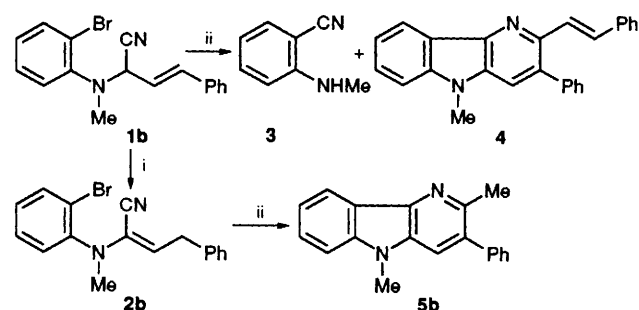
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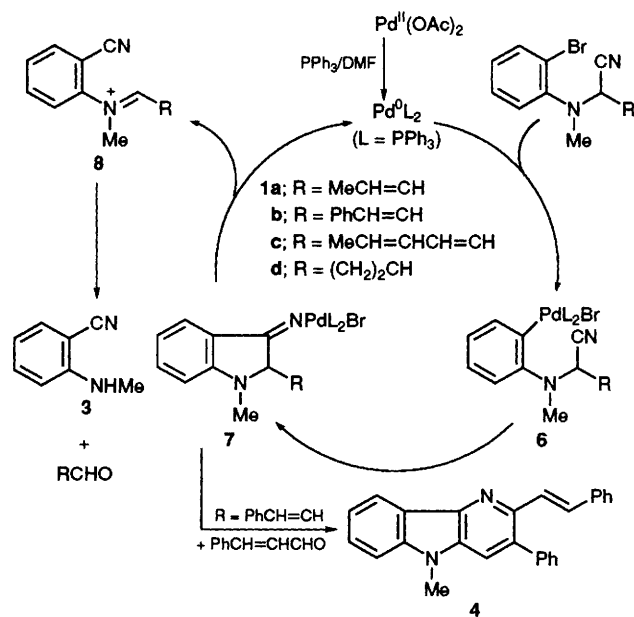
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$\alpha$ -(*o*-Bromoanilino)alkenenitriles are converted to 2-(methylamino)benzonitrile and varied  $\gamma$ -carbolines by catalysis with palladium; the reactions may involve intramolecular aryl additions to the cyano group and other processes such as cyano group transposition, electrocyclicisation, ethyl group transfer and oxidative aromatisation.

Heck reactions are important palladium-catalysed reactions for carbon-carbon bond formation such as the well documented arylation of olefins;<sup>1</sup> the corresponding arylation of a cyano group is, however, not reported. Our investigation of the palladium-catalysed cyclisations of varied  $\alpha$ -(*o*-bromoanilino)alkenenitriles **1** and **2** showed that the reactions occurred exclusively at the cyano group to give 2-(methylamino)benzonitrile<sup>2</sup> **3** and  $\gamma$ -carbolines<sup>3</sup> **4** and **5** (Scheme 1). Non-conjugated alkenenitriles **1a-c** were prepared,<sup>4</sup> by condensation of equimolar amounts of an appropriate unsaturated aldehyde, potassium cyanide, *N*-methyl-*o*-bromoaniline<sup>5</sup> and hydrochloric acid (12 mol dm<sup>-3</sup>). By a similar procedure, **1d** was prepared in 78% yield from cyclopropanecarbaldehyde. Treatment of **1a-c** with the strong base Bu<sup>t</sup>OK in Bu<sup>t</sup>OH-THF at 0 °C gave the more stable conjugated  $\alpha$ -amino alkenenitriles **2a-c** having the *2E*-configuration.<sup>6</sup> In a typical



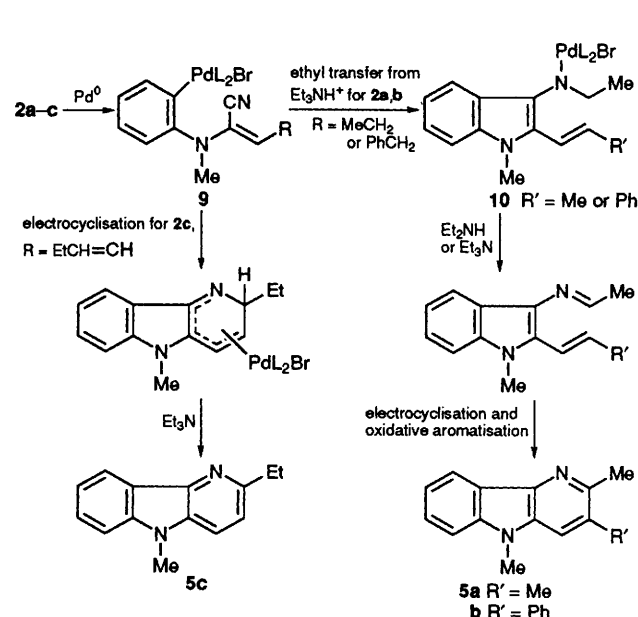
**Scheme 1** Reagents and conditions: i, Bu<sup>t</sup>OK (1 equiv.), Bu<sup>t</sup>OH-THF, 0 °C, 1 h; ii, Pd(OAc)<sub>2</sub>, Ph<sub>3</sub>P, Et<sub>3</sub>N, DMF, 100 °C, 6 h



**Scheme 2**

procedure, **1b** (1 mmol) in DMF (15 ml) was treated with Pd(OAc)<sub>2</sub> (0.1 mmol), Ph<sub>3</sub>P (0.2 mmol) and Et<sub>3</sub>N (1.2 mmol) for 6 h at 100 °C under an argon atmosphere.<sup>7</sup> The reaction mixture was cooled and EtOAc (30 ml) was added. The mixture was washed with water, the organic phase was concentrated and chromatographed on a silica-gel column by elution with gradients of EtOAc-hexane to give 2-(methylamino)benzonitrile **3** and  $\gamma$ -carboline **4** in 38 and 36% yields, respectively. Benzonitrile **3** was also obtained in 72–85% yields from the reactions of **1a**, **1c** and **1d**. The palladium-catalysed reactions of **2a-c** afforded  $\gamma$ -carbolines **5a-c** in 75–88% yields. The structures of **4** and **5** were rigorously determined.<sup>†</sup>

The mechanisms for the present palladium-catalysed reactions are not fully understood. The reactions of **1a-d** are presumably initiated by oxidative insertion of Pd<sup>0</sup> to the bromophenyl groups (Scheme 2). The organopalladium **6** undergoes cyclisation by attacking at the cyano group, giving **7**, but not at the olefinic double bonds. The iminoindoline **7** may rupture to an iminium ion **8**, which is subsequently hydrolysed to give 2-(methylamino)benzonitrile and aldehyde RCHO. When R is a styryl group, **7** may react further with cinnamaldehyde to give  $\gamma$ -carboline **4**. Compounds **2a-c** also undergo oxidative insertions with Pd<sup>0</sup>, giving the intermediates **9**. For **2c** (R is a butenyl group), a 6 $\pi$  electrocyclicisation and subsequent elimination of hydridopalladium produce  $\gamma$ -carboline **5c**. Though the intermediate **9** derived from **2a,b** (R = Et or PhCH<sub>2</sub>) cannot undergo electrocyclicisation, it may take an ethyl group from Et<sub>3</sub>NH<sup>+</sup>, giving **10**. Subsequent elimination of hydridopalladium, electrocyclicisation and oxidative aromatisation would furnish the  $\gamma$ -carbolines **5a,b** (Scheme 3).



**Scheme 3**

Our study of the palladium-catalysed reactions shows three uncommon features: (i) transposition of the cyano group in conversion of **1a-d** to **3**, (ii) two covalent bonds are formed in conversion of **2c** to **5c** by consecutive aryl-cyano addition and electrocyclisation, and (iii) involvement of an ethyl group transfer in conversion of **2a,b** to **5a,b**.

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#### Footnote

† All new compounds gave satisfactory spectral and analytical data.

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