**Introduction and Aim**

Suzuki (sp2-sp2) coupling and Buchwald coupling reactions are widely used in fine organic synthesis. It was found by us that Pd(dppf)-based catalysts were not applicable for automated synthesis because of difficult HT HPLC purification of products. Combinations of phosphine ligands with Pd2(dba)3 did not give predictable results due to uncontrolled degradation of Pd2(dba)3. Optimal results were achieved using G3 and G4 Buchwald precatalysts, but use of G4Xphos did not show statistically significant advantages on comparison of the product yield and precatalyst production cost. This finding was the reason for development of in-house laboratory scale up synthesis (up to 50 g from one synthetic run) and routine QC protocols of G3 and G4 Buchwald precatalysts.

**Catalysts QC by 1H NMR spectroscopy**

It was found that synthesis of Buchwald precatalysts in CH2Cl2 was not desirable because solvate molecules of CH2Cl2 reduced product yields in further coupling reactions. By analysis of NMR spectra of in-house-made samples it was found that the main impurities were:

(i) unreacted dimer; (ii) THF; (iii) n-hexane. For example, in Pd(G3)XPhos, except OCH3 signal of THF (C on the Fig.), the signals of impurities overlapped with the signals of the precatalyst: G3 dimer – B and D, hexane – F and G, THF – E.

<table>
<thead>
<tr>
<th>Precatalysts</th>
<th>Signal</th>
<th>Formula/ Conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>G3Xphos</td>
<td>2.5%</td>
<td>n-hexane – F, G</td>
</tr>
<tr>
<td>G3RuPhos</td>
<td>14.1%</td>
<td>G3 dimer – B, D</td>
</tr>
<tr>
<td>G3XantPhos</td>
<td>6.8%</td>
<td>THF - E</td>
</tr>
</tbody>
</table>

It was shown that G3, G4 Buchwald precatalysts could be used in automated milligram-scale synthesis by Suzuki and Buchwald reactions with HT HPLC purification, in contrast to the catalysts of earlier generations. Multi-gram protocol for synthesis of G3, G4 precatalysts was developed, QC method was proposed.

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**Conclusion**

It was shown that G3, G4 Buchwald precatalysts could be used in automated milligram-scale synthesis by Suzuki and Buchwald reactions with HT HPLC purification, in contrast to the catalysts of earlier generations. Multi-gram protocol for synthesis of G3, G4 precatalysts was developed, QC method was proposed.