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Conversion of alcohols into *N*-alkyl anilines *via* an indirect aza-Wittig reaction

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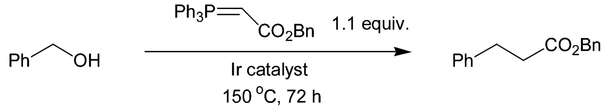
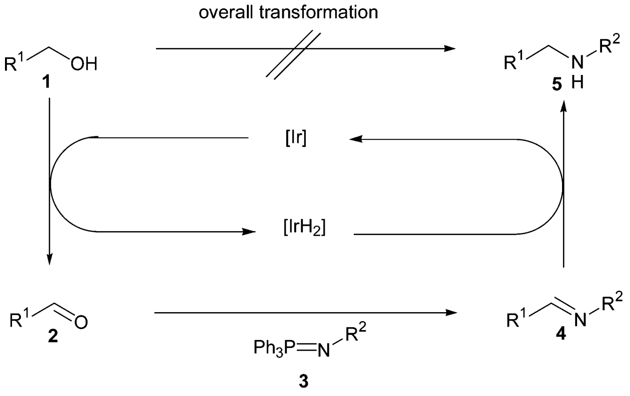
Iridium catalysed oxidation of alcohols provides the aldehydes required for *in situ* aza-Wittig reactions and the so-formed imines are reduced to amines under the reaction conditions.

We have recently demonstrated that alcohols can be used for indirect Wittig reactions. For example, benzyl alcohol is oxidised by an iridium[1] or ruthenium[2] catalyst to provide the corresponding aldehyde, which undergoes Wittig olefination, and subsequent *in situ* alkene reduction, as shown in Scheme 1.

Herein, we report the extension of this methodology to an indirect aza-Wittig reaction[3] according to Scheme 2. A substrate alcohol **1** can be activated by dehydrogenation to afford an intermediate carbonyl compound **2**. The activated substrate then can be transformed into imine **4**, *via* an aza-Wittig reaction between the aldehyde **2** and an iminophosphorane **3**. Hydrogenation of the intermediate **4** provides an indirect route for the conversion of alcohol **1** into the amine product **5**. Overall, the hydrogen "borrowed" in the oxidation of alcohol is returned in the reduction of the imine.



Scheme 1 Catalytic electronic activation: indirect Wittig reaction of benzyl alcohol.



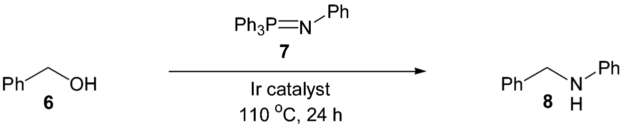
Scheme 2 Indirect aza-Wittig reactions upon alcohols.

Reduction of imines by transfer hydrogenation is a known process[4] and the conversion of alcohols into amines has been reported with ruthenium[5] and iridium catalysts.[6] To the best of our knowledge the aza-Wittig reaction has not been used for this process.

We examined the conversion of benzyl alcohol **6** into amine **8** using iminophosphorane **7** with Ishii's[7] iridium catalyst $[Ir(COD)Cl]_2$/phosphine and with the ruthenium catalyst $Ru(PPh_3)_3(CO)H_2$,[2] as shown in Scheme 3 and Table 1. Whilst the reaction involving 1,3-bis(diphenylphosphino)propane (dppp) and Cs_2CO_3 proved to be satisfactory, we found that the use of 1,1′-bis(diphenylphosphino)ferrocene (dppf) and K_2CO_3 afforded somewhat better results. It is interesting to note that these reactions proceeded under milder conditions (110 °C/24 h) than the corresponding indirect Wittig reactions, which required 150 °C/72 h.[1] The use of the ruthenium catalyst $Ru(PPh_3)_3(CO)H_2$ was also successful. However we decided to use the Ir/dppf catalyst in subsequent reactions.

Thus, benzylic alcohols **6**, **9** and **10**, as well as furfuryl alcohol **13** and the non-benzylic alcohol **15** were all converted successfully into the corresponding *N*-phenylamines, with isolated yields between 38–91% (Scheme 4).

A typical procedure for indirect aza-Wittig reactions: To a purged pressure tube containing $[IrCl(COD)]_2$ (0.016 g, 0.02 mmol), dppf (0.027 g, 0.05 mmol), K_2CO_3 (0.006 g, 0.05 mmol) and *N*-(triphenylphosphoranylidene)aniline (0.388 g, 1.1 mmol), was added benzyl alcohol (0.108 g, 1.0 mmol, 103 μL), followed by anhydrous toluene (1 mL). The tube was sealed and then heated at 110 °C for 24 h. The resulting brown mixture was poured into water (50 mL) and extracted with diethyl ether (3 × 50 mL). The combined organic extracts were washed with saturated brine (100 mL), dried ($MgSO_4$) and concentrated *in vacuo*. Purification by flash column chromatography (SiO_2, 40 : 1 petroleum ether (b.p. 40–60 °C)/diethyl ether) afforded the product as an oil (0.166 g, 91% yield).



Scheme 3 Iridium catalysed indirect aza-Wittig reactions with iminophosphorane **7**.

Table 1 Catalysts and conditions for aza-Wittig reaction of benzyl alcohol **6**[a]

Catalyst (mol%)	Ligand (mol%)	Base (mol%)	*T*/°C	*t*/h	Conversion (%)
$[Ir(COD)Cl]_2$ (2.5)	dppp (2.5)	Cs_2CO_3 (2.5)	150	72	90
$[Ir(COD)Cl]_2$ (2.5)	dppp (2.5)	Cs_2CO_3 (2.5)	110	24	60
$[Ir(COD)Cl]_2$ (2.5)	PPh_3 (5)	Cs_2CO_3 (2.5)	110	24	6
$[Ir(COD)Cl]_2$ (2.5)	dppp (2.5)	K_2CO_3 (5)	110	24	72
$[Ir(COD)Cl]_2$ (2.5)	dppf (5)	K_2CO_3 (5)	110	24	93
$Ru(PPh_3)_3(CO)H_2$ (1)	—	—	150	24	40

[a] Total conversion of benzyl alcohol **6** into compound **8** measured by analysis of the ¹H NMR spectra.

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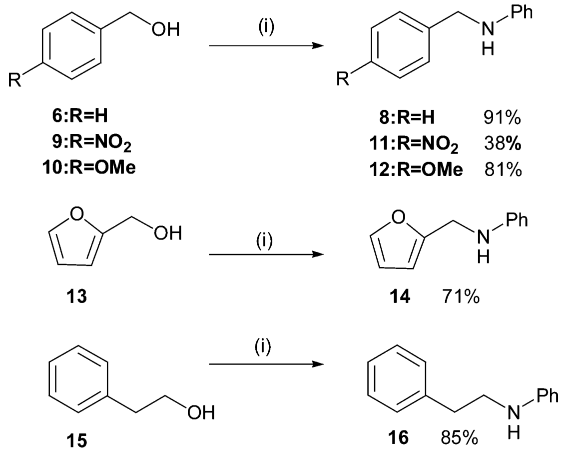
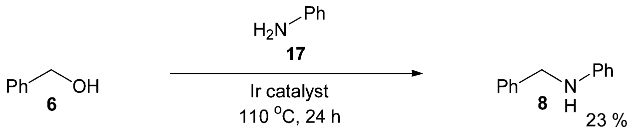
In addition to the aza-Wittig chemistry, it also proved to be possible to convert benzyl alcohol **6** into the amine **8** using aniline and iridium catalyst $[Ir(COD)Cl]_2$, as shown in Scheme 5.



Scheme 4 Synthesis of indirect aza-Wittig reaction adducts. Conditions: (i) $Ph_3P{=}NPh$, 1.1 equiv., $[IrCl(COD)]_2$, 2 mol%, dppf, 5 mol%, K_2CO_3, 5 mol%, PhMe, 1.00 M, 110 °C, 24 h.



Scheme 5 Preparation of *N*-phenylamines using aniline **17**.

However, the indirect aza-Wittig reaction provided better yields.

In summary, we have shown that it is possible to use iridium catalysts to convert alcohols into *N*-phenylamines *via* an indirect aza-Wittig reaction.

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