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The Use of $Ni(CO)_2(PPh_3)_2$ in Aryl and Pyridyl Coupling Reactions

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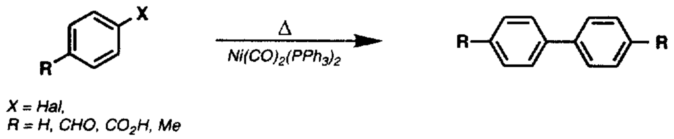
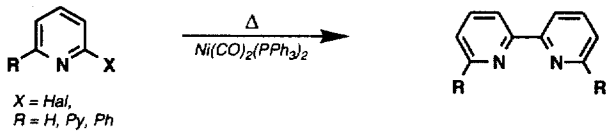
The zerovalent nickel complex $Ni(CO)_2(PPh_3)_2$ has been used for the coupling of aryl halides to form biaryls and for the coupling of bromopyridines to form polypyridines. The effects of solvent, halide and substituents have also been investigated. © 1999 Elsevier Science Ltd. All rights reserved.

Keywords: Nickel, Coupling reactions, Aryl halides, Biaryls, Pyridines

Transition-metal catalysed cross-coupling reactions are an extremely powerful tool in organic synthesis, being particularly useful for the generation of biaryls.[1] There have been a range of synthetic methodologies developed for metal-mediated biaryl synthesis, examples being direct oxidative dehydrodimerisation by Pd or Cu catalysts or reductive coupling with loss of a substituent group.[2] However, there are often complications with the reactions such as the harsh reaction conditions needed and the contamination of the desired biaryl with by-products.[3] In this article we show that, using the zerovalent nickel catalyst $Ni(CO)_2(PPh_3)_2$, aryl halides can be coupled to form biaryls efficiently under relatively mild conditions. In addition, polypyridine and aryl substituted pyridine complexes have been prepared using this catalyst. Reported here are just a few examples of the possible biaryl coupling reactions using $Ni(CO)_2(PPh_3)_2$, in order to illustrate the scope of the reagent.





PII: S0040-4039(99)00695-4

Thermolysis of aryl halides with $Ni(CO)_2(PPh_3)_2$ yields the corresponding biaryl.[4] The effects of solvent, halide and substituents on the coupling reaction were studied. The results are shown in the Table. The key findings are that:

1) The coupling process was found to go faster and give greater yields of product in polar solvents such as DMF and DMSO as opposed to non-polar solvents like n-hexane. This is not totally unexpected as the Ni(II) complexes formed in the oxidative addition steps of the reaction are much better solvated in polar media as compared to non-polar solvents.

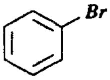
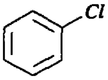
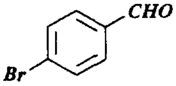
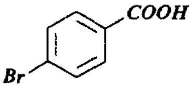
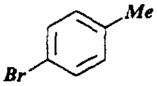
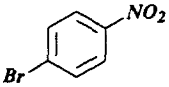
2) Although $Ni(CO)_2(PPh_3)_2$ can be used for the coupling of aryl chlorides, the bromides give far better results under the conditions used here. This may be due to the fact that, in the aryl halides, the more labile C-Br bond is activated more easily than the less labile C-Cl bond under the relatively mild conditions used here.

3) Aryl halides with electron withdrawing or weakly electron donating groups give high yields of biaryl. Of the substituted aryl halides studied, only *p*-bromonitrobenzene resulted in significant change in reactivity, no coupled products being formed.

In addition to symmetrically substituted biphenyls, it has been possible to develop the process for the synthesis of heterocyclic complexes, specifically substituted pyridines and polypyridines. Reaction of $Ni(CO)_2(PPh_3)_2$ with 2-bromopyridine in 1 : 1 toluene : DMF at 70 °C proceeds to give 2,2'-bipyridine in 75% yield within 4 hours. Similarly, 2-bromo-2,2'-bipyridine can be coupled to yield quaterpyridine (70% yield).[5] This offers a new route to the synthesis of a range of oligopyridine ligands many of which would otherwise require a number of low yielding steps for synthesis. Sterically hindered molecules such as 6,6'-diphenyl-2,2'-bipyridine can also be synthesised by this route, reaction of 2-bromo-6-phenyl-pyridine with the Ni(0) complex giving the coupled product in 70% yield.[6] Unlike many of the previous reports of metal-mediated polypyridine synthesis where the heterocycle coordinates to the metal and hence requires a lengthy work-up,[7] in our studies the polypyridine seems not to coordinate and is easily obtained from the reaction mixture.

In summary, we have utilised the Ni(0) complex $Ni(CO)_2(PPh_3)_2$ for the synthesis of biaryls and polypyridines. We are not the first to employ zerovalent nickel complexes in coupling reactions.[8] However, we have found that, by using $Ni(CO)_2(PPh_3)_2$ it has been possible to overcome many of the problems associated with other Ni(0) complexes such as $Ni(COD)_2$ and $Ni(PPh_3)_4$, namely their extreme air and moisture sensitivity.

Table: Nickel mediated coupling of aryl halides a)

Substrate	Solvent	Reaction time (h)	Yield of biaryl b)
	DMSO	1	50
		3	70
		6	75
	toluene	1	40
		3	60
		6	65
	hexane	1	10
		3	15
		6	25
	DMSO	3	30
		6	35
	DMSO	3	50
		6	75
	toluene	3	40
		6	65
	hexane	3	40
		6	20
	DMSO	6	70
	DMSO	6	70
	DMSO	6	0
		12	0
		24	0

a) *All reactions are carried out at 70 °C using 0.03 mmol $Ni(CO)_2(PPh_3)_2$ and 10 mmol of aryl halide*

b) *Determined by GC*

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2. S.P. Stanforth, *Tetrahedron*, 1998, **39**, 263.

3. M. Moreno-Manas, M. Pérez and R. Pleixats, *J. Org. Chem.*, 1996, **61**, 2346.

4. The representative procedure is illustrated by the case of bromobenzene. Into a dry, nitrogen flushed flask was added DMF (20 ml), bromobenzene (1 ml, 6.25 mmol) and $Ni(CO)_2(PPh_3)_2$ (119 mg, 0.18 mmol) and the resultant reaction mixture heated to 70 °C. The colour of the solution changed over time from light yellow to red-brown and then into greenish blue. The amount of biphenyl formed was determined periodically by GC analysis of the reaction mixture, comparing the retention time with that of a commerically avaliable sample of biaryl.

5. Characterised by comparison of spectral data with that in the literature (Y. Uchida, R. Kajita, Y. Kawasaki and S. Oae, *Tetrahedron Lett.*, 1995, **36**, 4077)

6. Characterised by comparison of spectral data with that in the literature (E.C. Constable, S.M. Elder, J. Healy and D.A. Tocher, *J. Chem. Soc., Dalton Trans.*, 1990, 1669)

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