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Lithium Hydride Mediated Nickel(0) Catalysed Biaryl Synthesis from Aryl Chlorides and Bromides†

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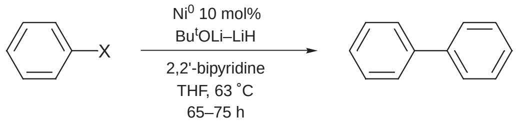
Lithium hydride is efficiently used as a reducing agent in the ligated Ni^0 catalysed homocoupling of aryl bromides and chlorides.

Biaryls have a large number of physical and chemical properties and have found many applications in industrial, biological or polymer chemistry.[1–4] The metal promoted homocoupling reaction of aryl halides or sulfonates is traditionally accomplished by the well known Ullmann reaction[5] or by a metal catalysed coupling reaction.[6] In this context, the nickel induced homocoupling of aryl derivatives has received considerable attention during the last decades because the reaction tolerates a large variety of functional groups and proceeds under mild conditions.[7] For our part, we have already reported homocouplings of aryls and heteroaryl bromides and chlorides in the presence of stoichiometric amounts of NiCRA-L[8] constituted of ligated Ni^0 *in situ* generated by reduction of $Ni(OAc)_2$ with activated sodium hydride.[9] Attempts to catalytically use these reagents failed due to significant reduction of the starting materials. Following our preliminary work on the activation of lithium hydride,[10] we now report that activated LiH can be efficiently used as a reducing agent in the catalytic cycle of biaryl synthesis from aryl halides.

We firstly found that biphenyl can be efficiently obtained in refluxing THF from bromo- or chlorobenzene using 10 mol% of a $[Ni^0/bpy]$ catalyst in the presence of an excess of Bu^tOLi activated LiH (Scheme 1).



	Isolated yield (%)
X = Br	92
Cl	89

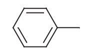
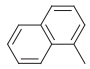
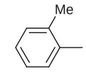
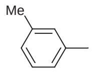
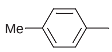
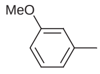
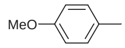
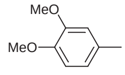
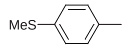
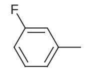
Scheme 1

Good coupling yields (respectively 92 and 89% isolated) were obtained when: (i) 20 equiv., of LiH relative to Ni^0 were used. A larger excess (30 equiv.) did not improve yields or reduce reaction times while 10 equiv. led to an incomplete reaction; (ii) 2 equiv. of Bu^tOLi relative to Ni^0 were employed; (iii) 4 equiv. of 2,2′-bipyridine relative to Ni^0 were used. Note that 2,2′-bipyridine is easily recovered during the work-up procedure of the reaction.

We applied these catalytic conditions to the homocoupling of substituted aryl bromides (Table 1). Good yields of biaryls were obtained when the aryl bromide is substituted by electron-withdrawing groups such as 3-F or 3-MeO (runs 6 and 10) while for substrates having an electron-donating group such as 4-MeO, the reaction is greatly retarded and only poor yields of coupling products could be obtained (run 7). 4-Bromoveratrol (run 8) coupled in 75% yield due to the antagonist effects of the 3- and 4-MeO substituents. These results are consistent with those classically obtained in Pd^0 or Ni^0 induced coupling reactions.[6,7] A particular behaviour was observed with sulfur containing aryl bromide (run 9). Only 10% of biphenyl derivative was observed by GC. This corresponded to only one cycle of Ni^0. It may be assumed that this limitation is due to a competitive desulfurisation[11] which poisoned the catalyst. Finally, the reaction is tolerant of *ortho* substitution. Indeed, 2,2′-dimethylbiphenyl is formed in 61% isolated yield (run 3). In all cases, the reactions were very clean. It appears that the ligated Ni^0-activated LiH system exhibited no reducing properties towards the starting materials in contrast to those prepared with NaH[9] and aside from the coupling product materials were recovered at the end of the reaction. It is also noteworthy that classical conditions known to improve homocoupling yields are inef-

Table 1 Homocoupling of aryl bromides using a Ni^0 catalyst and LiH^a

$$2\,ArBr \xrightarrow[2,2'\text{-bipyridine, THF, }63\,^\circ C]{Ni(OAc)_2\ 10\text{ mol\%, }Bu^tOLi,\ LiH} Ar\text{-}Ar$$

Run	Ar	t/h	Yield(%) GC	Yield(%) Isolated[b]
1		68	100	91
2		71	87	88
3	 	77	76	61
4	 	66	100	92
5	 	80	93	74
6	 	71	100	93
7	 	93	47	39
8	 	74	91	75
9	 	82	10	—
10	 	71	100	87

[a] Aryl halide (25 mmol), $Ni(OAc)_2$ (2.5 mmmol), LiH (55 mmol), Bu^tOH (5 mmol) and 2,2′-bipyridine (10 mmol) were used. [b] Isolated yields after chromatography on silica gel.

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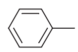
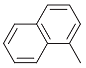
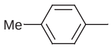
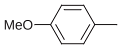
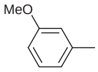
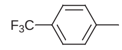
† This is a **Short Paper** as defined in the Instructions for Authors, Section 5.0 [see *J. Chem. Research (S)*, 1999, Issue 1]; there is therefore no corresponding material in *J. Chem. Research (M)*.

Table 2 Homocoupling of chloroarenes (ArCl) using a Ni^0 catalyst[a]

		10 mol% Ni^0			20 mol% Ni^0		
			Yield(%)			Yield(%)	
Run	Ar	t/h	GC	Isolated[b]	t/h	GC	Isolated[b]
1		82	94	89	—	—	—
2		107	31	27	65	91	87
3		104	73	59	50	94	91
4		—	—	—	65	68	63
5		83	79	70	—	—	—
6		95	14	—	62	86	84

[a] Reactions performed on 25 mmol aryl chloride. [b] Isolated yields after chromatography on silica gel.

ficient with our system. For example, performing the reaction in refluxing DME or toluene or adding potassium iodide (0.2 equiv. relative to the aryl bromide) did not accelerate the catalytic cycle. Then, the Ni^0 regeneration induced by the alkoxide activated lithium hydride seems to be the rate limiting step in our process.

It was next of interest to study the homocoupling of chloroarenes which are inexpensive and readily available substrates. Results obtained are summarized in Table 2. Good yields in homocouplings were generally obtained. However and as previously observed with bromoarenes, it appeared that aryl chlorides substituted by electron-donating groups gave poor yields of biaryls and that a 10 mol% Ni^0 catalyst seemed to be insufficient to complete the reaction, even with aryl chlorides bearing no electron-donating substituent. Then a higher concentration of catalyst (20 mol%) is necessary to achieve good yields of biaryls. We make the assumption that *in situ* generated salt (LiCl) could modify the nature of the catalyst and inhibit its regeneration.[12]

In summary, we have found that homocoupling of aryl halides can be efficiently obtained using a lithium hydride containing Ni^0 catalyst. We anticipate that this method is likely to find use in organic chemistry since LiH and our Ni^0 catalyst are non-pyrophoric, easy to prepare and to handle and of low cost.

Experimental

All experiments were carried out under a nitrogen atmosphere. THF was distilled from benzophenone ketyl. Crushed $Ni(OAc)_2 \cdot 6\,H_2O$ was dried for 12 h at 110 °C before use. 2,2′-Bipyridine was recrystallised in hexane before use. All reagents were purchased from commercial sources and were used without purification. Melting points were taken on a Tottoli apparatus and were uncorrected. Gas chromatographic analyses were conducted on a Shimadzu GC-8A instrument equipped with a flame-ionisation detector and employing an Alltech EC5 column ($30\,m \times 0.32\,mm \times 2.65\,\mu m$ thickness). Column chromatography was carried out using Kieselgel (70-230 mesh).

General Procedure for the Ni^0-catalysed Homocouplings of Aryl Halides.—Under a nitrogen atmosphere, *tert*-butyl alcohol (5 mmol, 0.370 g) in 5 ml was added to lithium hydride (55 mmol, 0.440 g) in 20 ml THF and the mixture was refluxed overnight. Dried $Ni(OAc)_2$ (2.5 mmol, 0.44 g) and 2,2′-bipyridine (10 mmol, 1.56 g) were then added. After stirring for 1 h at reflux, the aryl halide (25 mmol) in 5 ml THF was added dropwise to the dark ligated Ni^0 complex. The reaction was monitored by GC analysis of small aliquats. The internal standard was hydrocarbon ($C_{10}-C_{12}$). After completion of the reaction, excess hydride was destroyed by dropwise addition of water at 25 °C. The mixture was filtered, dried over $MgSO_4$ and evaporated under reduced pressure. The biaryl was obtained after column chromatography on silica gel. All biaryls were fully characterized by their spectroscopic data (^1H and ^{13}C NMR) and their purity was established by comparison with published melting point or found to be higher than 99% by GC.

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References

1 U. Anton, C. Göltner and K. Mullen, *Chem. Ber.*, 1992, **125**, 2325.
2 B. H. Lipschutz, P. Müller and D. Leinweber, *Tetrahedron Lett.*, 1999, **40**, 3677.
3 K. Mamikawa, T. Watanabe and M. Uemura, *J. Org. Chem.*, 1996, **61**, 1375.
4 (*a*) T. Yamamoto, A. Morita, Y. Miyazaki, T. Maruyama, H. Wakayama, Z. H. Zhou, Y. Nakamura, T. Kanbara, S. Sasaki and K. Kubota, *Macromolecules*, 1992, **25**, 1214; (*b*) S. S. Zhu and T. M. Swager, *Adv. Mater.*, 1996, **8**, 497; (*c*) N. E. Leadbeater and S. M. Resouly, *Tetrahedron Lett.*, 1999, **40**, 4243.
5 (*a*) F. Ullmann, *Ber.*, 1903, **36**, 2389; (*b*) E. Fanta, *Synthesis*, 1974, **1**, 9.
6 (*a*) N. Miyaura and A. Suzuki, *Chem. Rev.*, 1995, **95**, 2457; (*b*) V. Farina, *Pure Appl. Chem.*, 1996, **68**, 73.
7 (*a*) M. F. Semmelhack, P. M. Helquist, L. D. Jones, L. Keller, L. Mendelson, L. S. Ryono, J. G. Smith and R. D. Stauffer, *J. Am. Chem. Soc.*, 1981, **103**, 6460; (*b*) L. Colon and D. R. Kelsey, *J. Org. Chem.*, 1986, **51**, 2627: (*c*) A. Jutand and A. Mosleh, *Synlett*, 1993, 568; (*d*) V. Percec, J. Y. Bae, M. Zhao and D. H. Hill, *J. Org. Chem.*, 1995, **60**, 1060 and 1066; (*e*) H. A. Reisch, V. Enkelmann and U. Scherf, *J. Org. Chem.*, 1999, **64**, 655.
8 P. Caubère, *Pure Appl. Chem.*, 1985, **57**, 1875; (*b*) P. Caubère, *Rev. Heteroat. Chem.*, 1991, **4**, 79; (*c*) P. Gallezot, C. Leclercq, Y. Fort and P. Caubère, *J. Mol. Catal.*, 1994, **93**, 79.
9 M. Lourak, R. Vanderesse Y. Fort and P. Caubère, *J. Org. Chem.*, 1989, **54**, 4840; (*b*) M. Lourak, R. Vanderesse, Y. Fort and P. Caubère, *J. Org. Chem.*, 1989, **54**, 4844. (*c*) Y. Fort S. Becker and P. Caubère, *Tetrahedron.*, 1994, **50**, 11893.
10 Y. Fort, *Tetrahedron Lett.*, 1995, **36**, 6051.
11 Ligated Ni^0 reagents were found to be very efficient in desulfurization of various sulfur containing compounds: (*a*) S. Becker, Y. Fort, R. Vanderesse and P. Caubere, *J. Org. Chem.*, 1989, **54**, 4848; (*b*) S. Becker, Y. Fort and P. Caubere, *J. Org. Chem.*, 1990, **55**, 6194; (*c*) C. Kuehm-Caubere, A. Guilmart, S. Adach-Becker, Y. Fort and P. Caubere, *Tetrahedron Lett.*, 1998, **39**, 8987.
12 In the presence of LiCl, the catalyst is difficult to prepare. Moreover, generation of our catalyst from $NiCl_2$ is more difficult than from $Ni(OAc)_2$: S. Illy, O. Tillement, F. Machizaud, J. M. Dubois, F. Massicot, Y. Fort and J. Ghanbaja, *Philas. Mag. A*, 1999, **79**, 1021.