

IN SITU GENERATION OF A SOLVATED ZEROVALENT NICKEL REAGENT. BIARYL FORMATION

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(Received in USA 7 July 1975; received in UK for publication 22 August 1975)

Zerovalent nickel reagents offer prolific new areas of synthetic organic methodology. Bis(1,5-cyclooctadiene)nickel(0) [Ni(COD)₂] and tetrakis(triphenylphosphine)nickel(0) [Ni(TPP)₄] have mediated the symmetric coupling of aryl^{1a,b} and vinyl² halides. However, these sensitive reagents are conventionally prepared by cumbersome techniques involving trialkyl- or dialkylalkoxyaluminum species as reducing agents under vacuum line or dry-box conditions.^{3a,b,12} To circumvent these limitations we have devised a simple method for the in situ generation and routine utilization of tris(triphenylphosphine)nickel(0) [Ni(TPP)₃] for halide coupling in organic synthesis.

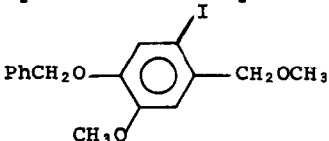
Coordinately unsaturated Ni(TPP)₃, formed in solution from Ni(TPP)₄ by ligand dissociation^{4a,b} is most likely the reactive species undergoing oxidative addition⁵ in reactions of Ni(TPP)₄ with aryl halides.^{1b,c3b,6} We felt it would be possible to reduce bis(triphenylphosphine)nickel(II)dichloride⁷ with zinc in the presence of triphenylphosphine, generating Ni(TPP)₃ in situ,^{4a} and then to use the solution of zerovalent nickel complex for specific organic transformations. These expectations were justified, and we have shown that Ni(TPP)₃ thus formed, followed by treatment with aryl halides, produces biaryls in good to excellent yields (Equation 1).



A typical procedure follows: Into a flamed 25 ml round bottom flask are placed (TPP)₂NiCl₂ (653 mg, 1.0 mmole), triphenylphosphine (524 mg, 2.0 mmole), and zinc powder (66 mg, 1.0 mmole). A septum cap is placed on the flask, 5 mls of dry, O₂-free dimethylformamide are added and the flask is evacuated and filled with N₂ three times by means of one syringe needle connected

with Tygon tubing to an aspirator and another syringe needle connected to a nitrogen line. The flask is then placed in an oil at 50°C and rapidly stirred for 1 hr. During the first 15 min. the initially deep blue solution turns deep green, then light green-yellow and finally yields the characteristic red-brown slurry of Ni(TPP)₃. Methyl m-bromobenzoate (215 mg, 1.0 mmole) in 2 mls of dry, O₂-free dimethylformamide is added via syringe with careful exclusion of air and the reaction mixture is stirred under nitrogen at 50°C for 24 hrs. It is then cooled, poured into 20 mls 2% HCl, extracted into 30 mls chloroform, diluted with 30 mls diethyl ether, washed well with distilled water, then brine, then dried over magnesium sulfate. Filtration and removal of solvents yields a residue which is preparatively chromatographed on silica to yield 114 mg, 3,3'-dicarbomethoxybiphenyl (85%), mp 102-103.5° (lit. 104°). Table I lists some representative examples.

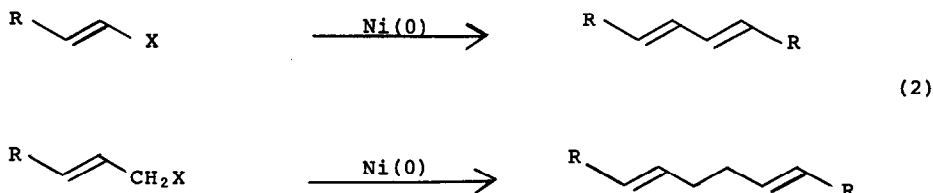
TABLE I

<u>Aryl Halide</u>	<u>Yield of Biaryl (%)^a</u>	<u>Mp^b</u>	<u>(Lit. mp)</u>
I. Bromobenzene	73	69- 71°	(71)°
II. p-Bromoanisole	42	171-174	(173)
III. p-Bromotoluene	60	115-117	(112)
IV. Methyl o-iodobenzoate	59	70-72	(74)
V. Methyl m-bromobenzoate	85	102-103.5	(104)
VI. Methyl p-bromobenzoate	76	208-212	(212-213)
VII. p-Bromoacetophenone	68	189-191	(192-193)
VIII. p-Bromobenzaldehyde	70	141-143	(145)
IX. 	68	111-114	-

- a. Yields are not optimized - products isolated by thick layer chromatography on silica gel plates and characterized by nmr, ir, mass spec, mp.
- b. Melting points are uncorrected and taken of the crude product from chromatography.

Aryl halides having two ortho substituents do not couple.⁸ In general,

dimethylformamide was the most suitable solvent found; however, it is interesting to note that in specific cases solvent influences were substantial. For instance, a 92% yield to 4,4'-diacetylbiphenyl of mp 190.5-191.5° (lit. 192-193°) was obtained by generating $\text{Ni}(\text{TPP})_3$ in pyridine and allowing it to react with p-bromoacetophenone for 12 hrs at 40°.



In addition to biaryl formation we have shown in situ prepared nickel(0) to couple vinyl and allylic halides (Equation 2). For example, β -bromostyrene (80% trans) in dimethylformamide was added to the $\text{Ni}(\text{TPP})_3$ slurry in dimethylformamide at -50° and was allowed to warm to ambient temperature, then stirred 18 hrs. After workup and chromatography a 43% yield of predominantly trans, trans 1,4-diphenylbutadiene was obtained. Under similar conditions cinnamyl chloride was coupled to bicinnamyl in 50% yield.⁹

This new procedure avoids the use of special techniques in the utilization of zerovalent nickel for halide-coupling reactions and may be of value in other transformations mediated by such species.^{1a,3a,6,10a,b,11}

Acknowledgement: We are grateful to the National Cancer Institute, U.S.P.H.S., for Grant CA-11326 in partial support of this investigation. L.S.L. thanks the University of Rochester for award of a Sherman-Clarke Fellowship.

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