J. Org. Chem. **2001,** *66,* 7539−7541 **7539**

Bis-Cyclopentadienyl Nickel (Nickelocene): A Convenient Starting Material for Reactions Catalyzed by Ni(0) Phosphine Complexes

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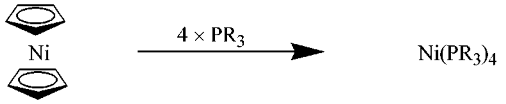
Received June 14, 2001

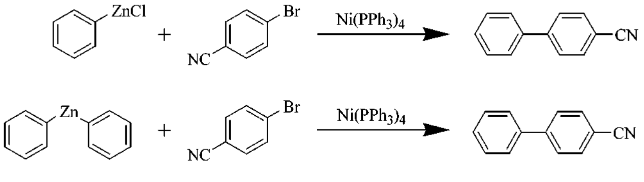
Nickel(0)-catalyzed carbon−carbon bond forming reactions are an extremely powerful tool in organic synthesis.[1−4] Using nickel(0) complexes it is often possible to invoke reactivity with substrates that are not activated by palladium analogues or else perform reactions using less forcing conditions. In addition, as palladium is now a very expensive metal commercially, nickel is a significantly cheaper alternative. The big disadvantage of using nickel(0) complexes is their air sensitivity, compounds such as $Ni(PPh_3)_4$ and $Ni(COD)_2$ [COD = 1,5-cyclooctadiene] having to be handled under strictly anaerobic conditions, which affects their popularity as catalysts. Chemists have tried to overcome this by reducing stable Ni(II) complexes to Ni(0) analogues in situ by adding, for example, an excess of zinc or butyllithium to the reaction mixture or in a premixture.[5,6] This is far from ideal, as a large amount of waste can be produced and significant byproduct formation often occurs especially when delicate substrates are used. We report here the use of bis-cyclopentadienyl nickel (nickelocene) as a starting material for Ni(0)-catalyzed reactions and demonstrate its applicability in a range of reactions with precedents in the literature so direct comparisons between experimental procedures and yields can be made.

The chemistry of nickelocene ($NiCp_2$) was explored in the 1960s by Werner and others but its potential use as a precatalyst for metal-mediated organic synthesis has never been exploited.[7] It is commercially available[8] or else readily prepared in high yield from cyclopentadiene and $NiCl_2$.[9] It is air and moisture stable, although when stored for prolonged periods of time should be kept under a nitrogen atmosphere. Unlike other metallocenes such as $M(C_5H_5)_2$ [M = V, Cr, Ru, Os], nickelocene reacts with tertiary mono phosphine and phosphite ligands, PR_3, to form M(0) complexes $Ni(PR_3)_4$.[10] It is this reactivity that we have exploited here for the in-situ generation of an active catalyst.



We find that the complexes are best formed by direct reaction of nickelocene and the pure ligand in the absence of solvent. The mixture is heated to around 80 °C in a Schlenk tube under strictly anaerobic conditions for a few minutes, which leads to a near quantitative yield of $Ni(PR_3)_4$. Alternatively, the preparation can also be effected by addition of ligand to a degassed solution of nickelocene followed by heating. Again, within a few minutes a near quantitative yield of $Ni(PR_3)_4$ is obtained. The solution-phase reaction works equally well in a range of hydrocarbon-based media but some problems occur in solvents bearing ether linkages. In the majority of cases we find that it is better to prepare the Ni(0) complex by the direct reaction route, as this is faster and yields are nearer 100%. Complexes have been prepared here with PPh_3, PCl_3, and $P(O^iPr)_3$ yielding $Ni(PPh_3)_4$, $Ni(PCl_3)_4$, and $Ni\{P(O^iPr)_3\}_4$, respectively, for the purposes of using them in catalysis.[11] To show that the Ni(0) complexes generated from nickelocene are active in catalysis, each has been used for a known reaction and the yields of product have been compared with those reported in the literature.

For use in the coupling of aryl or zinc reagents with aryl bromides,[12] the reagents, namely the aryl zinc and aryl bromide, can simply be added to a THF solution of $Ni(PPh_3)_4$ prepared from $NiCp_2$ and the resultant mixture stirred at room temperature for 2 h. As shown in Table 1, the results obtained are almost identical to those reported in the literature, as expected, since the active complex is the same in both cases. The synthesis of $Ni(PPh_3)_4$ from $NiCp_2$ for use in catalysis has significant advantages over the conventional preparation which involves reduction of nickel(II) acetylacetonate with triethylaluminum in the presence of triphenylphosphine where a yield of 55% of $Ni(PPh_3)_4$ is obtained.[13] It is therefore necessary to purify the phosphine complex before use. With the $NiCp_2$ route, no purification is needed so all catalyses can be performed in the same reaction vessel that the Ni(0) complex is prepared in.



The highly reactive complex $Ni(PCl_3)_4$ can be prepared from $NiCp_2$ and used successfully in the catalytic cyclo-

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[1] Bhaduri, S. Homogeneous Catalysis: Mechanisms and Industrial Applications, Wiley-Interscience: New York, 2000.

[2] Diederich, F., Stang, P., Eds.; Metal-Catalysed Cross Coupling Reactions, Wiley-VCH: Weinheim, 1998.

[3] Lipshutz, B. H.; Blomgren, P. A. *J. Am. Chem. Soc.* **1999**, *121*, 5819−5820.

[4] Chung, K.-G.; Miyake, Y.; Uemura, S. *J. Chem. Soc., Perkin Trans. 1* 2001, 2725−2729.

[5] Percec, V.; Bae, J.-Y.; Hill, D. H. *J. Org. Chem.* **1995**, *60*, 176−185.

[6] Saito, S.; Oh-Tani. S.; Miyaura, N. *J. Org. Chem.* **1997**, *62*, 8024−8030.

[7] For a discussion of early work on the chemistry of nickelocene, see Werner, H. *J. Organomet. Chem.* **1980**, *200*, 335−348.

[8] Nickelocene can be purchased from a range of chemical manufacturers including Strem and Sigma-Aldrich.

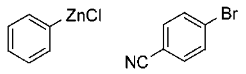
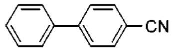
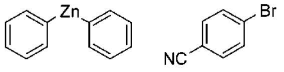
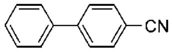
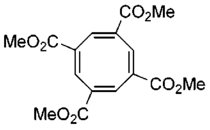
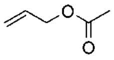
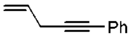
[9] Barnett, K. W. *J. Chem. Educ.* **1974**, *51*, 422.

[10] Olechowski, J. R.; McAlister, C. G.; Clark, R. F. *Inorg. Chem.* **1965**, *4*, 246.

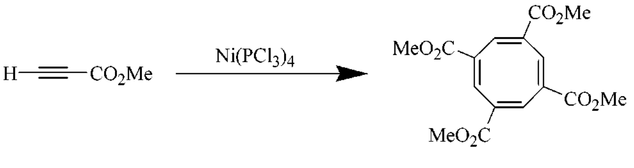
[11] On reaction of $NiCp_2$ with phosphines, the cyclopentadiene groups displaced dimerise to form pentafulvalene. In the cases we have studied we find that this does not seem to partake in any further reaction.

10.1021/jo0158377 CCC: $20.00

Table 1. Comparative Yields Using Literature Methods and Using Nickelocene as Catalyst Precursor

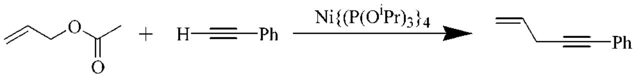
Starting materials	Product	Pre-Catalyst	Catalyst	Yield using $NiCp_2$ as pre-catalyst	Literature reported yield
		$NiCp_2 + PPh_3$	$Ni(PPh_3)_4$	87	90[12]
		$NiCp_2 + PPh_3$	$Ni(PPh_3)_4$	86	85[12]
$H{-}{\equiv}{-}CO_2Me$	 (and other isomers)	$NiCp_2 + PCl_3$	$Ni(PCl_3)_4$	49	55[14]
 $H{-}{\equiv}{-}Ph$		$NiCp_2 + P(O^iPr)_3$	$Ni\{(P(O^iPr)_3\}_4$	86	84[17]

tetramerization of methyl propiolate. The yield of product is slightly lower than that reported in the literature[14] (Table 1), this being attributed to some decomposition during the course of the reaction. $Ni(PCl_3)_4$ is highly oxygen and water sensitive in solution, and its synthesis by other routes involves either highly reactive Ni(0) precursors such as $Ni(allyl)_2$ or highly toxic $Ni(CO)_4$.[15,16] When preparing the $Ni(PCl_3)_4$, from nickelocene, to minimize any decomposition we find that the best route involves gentle heating (30 °C) of a pentane solution of $NiCp_2$ and PCl_3 for a few minutes. Removal of the pentane under reduced pressure gives a solid sample of the complex to which another solvent and reagents can be added for nickel-mediated catalysis, again making it a one-pot reaction.



(and other isomers)

In another attempt to show the advantages of using $NiCp_2$ as a starting material for Ni(0) complexes, $Ni\{P(O^iPr)_3\}_4$ was prepared by reaction with $P(O^iPr)_3$ and used in the catalytic formation of nonconjugated alkenynes from allylic esters of organic acids and alk-1-ynes. Again yields using the $NiCp_2$ route are analogous to those reported in the literature,[17] and again this route offers a convenient method of preparing the active Ni(0) complex which is otherwise most conveniently synthesized by the reaction of highly air and moisture sensitive $Ni(COD)_2$ with $P(O^iPr)_3$.[18]



From our findings, the advantages of using nickelocene as a starting material for metal-mediated catalysis are clear, and its applicability runs much further than the reactions presented here. Ni(0) complexes are used as catalysts in a wide range of organic transformations,[19] and we highlight here a route to their generation, avoiding many of the problems encountered to date. Work is currently underway to exploit this further.

Experimental Section

General. Reactions were carried out under a nitrogen atmosphere in oven-dried glassware. Nickelocene, PPh_3, PCl_3, and $P(O^iPr)_3$ were used as purchased. All liquid reagents for use in catalysis were degassed before use. Solvents were distilled and stored over molecular sieves. The ^1H- and $^{31}P\{^1H\}$-NMR spectra were recorded in $CDCl_3$ using a Bruker AVANCE 360 MHz spectrometer at 293 K and are referenced to trimethylsilane and phosphoric acid, respectively.

General Procedure for the Direct Synthesis of $Ni(PR_3)_4$ from Nickelocene. A Schlenk tube was charged with nickelocene and 4 equiv of PR_3 (R = Ph, O^iPr). After the tube was evacuated under vacuum and filled with nitrogen, the resultant mixture heated to 80 °C for 10 min after which time the $Ni(PR_3)_4$ complex was formed. Reactions were performed using 50 mg, 0.26 mmol nickelocene. The products were characterized by comparison of spectral and analytical data with that in the literature.[20]

Procedure for the Synthesis of $Ni(PCl_3)_4$ from Nickelocene. A Schlenk tube was charged with nickelocene (50 mg, 0.26 mmol) and 4 equiv of PCl_3 (143 mg, 0.09 mL, 1.04 mmol). After the tube was evacuated under vacuum and filled with nitrogen, freshly degassed dry pentane (10 mL) was added and the resultant mixture was heated to 30 °C for 10 min after which time the $Ni(PCl_3)_4$ complex was formed. The pentane was then

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(12) Negishi, E.-I.; King, A. O.; Okukado, N. *J. Org. Chem.* **1977**, *42*, 1821.

(13) Severson, S. J.; Cymbaluk, T. H.; Ernst, R. D.; Higashi, J. M.; Parry, R. W. *Inorg. Chem.* **1983**, *22*, 3834.

(14) Leto, J. R.; Leto, M. F. *J. Am. Chem. Soc.* **1961**, *83*, 2944.

(15) Seel, F.; Ballreich, K.; Schmutzler, R. *Chem. Ber.* **1961**, *94*, 1173.

(16) Chiusoli, G. P.; Pallini, L.; Terenghi, G. *Transition Met. Chem.* **1983**, *8*, 189.

(17) Catellani, M.; Chiusoli, G. P.; Salerno, G.; Dallatomasina, F. *J. Organomet. Chem.* **1978**, *146*, C19.

(18) Ittel, S. D. *Inorg. Synth.* **1990**, *28*, 98.

(19) See for example: Paqette, L. A., Ed. *Encyclopedia of Reagents for Organic Synthesis*; Pergamon: Chichester, 1995.

(20) Ittel, S. D. *Inorg. Synth.* **1990**, *28*, 98.

removed under vacuum, leaving a solid sample of the product. ^{31}P NMR: −172 ppm.

Representative Procedure for the Nickel-Catalyzed Cross-Coupling of Phenyl and Benzyl Zinc Chlorides with Bromobenzonitrile. A small Schlenk tube was charged with nickelocene (38 mg, 0.2 mmol) and PPh_3 (210 mg 0.8 mmol). After the tube was evacuated under vacuum and filled with nitrogen, the resultant mixture was heated to 80 °C for 10 min after which time dry THF (5 mL) was added and the solution of $Ni(PPh_3)_4$ allowed to cool to room temperature. To the cooled solution was added *p*-bromobenzonitrile (728 mg, 4 mmol) and a THF solution of phenylzinc chloride (4.4 mL of 1 M solution, 4.4 mmol). The reaction mixture was stirred at room temperature for 2 h after which time the mixture was worked up by diluting with ether (30 mL), stirring with 1 M HCl (3 × 10 mL additions), removing the organic layer, removing the solvent, redissolving in ether, filtering the solution, drying the ether with anhydrous $MgSO_4$, and concentration. Analysis of the product mixture by NMR in the presence of a standard showed that *p*-phenylbenzonitrile was formed in 87% yield. ^{1}H NMR: $\delta =$ 7.71 (m, 2H), 7.62 (m, 2H), 7.45 (m, 2H), 7.38 (m, 3H).

Procedure for the Nickel-Catalyzed Tetramerization of Methyl Propiolate. A small Schlenk tube was charged with nickelocene (38 mg, 0.2 mmol) and PCl_3 (110 mg, 0.069 mL, 0.8 mmol). After the tube was evacuated under vacuum and filled with nitrogen, pentane was added and the resultant mixture was heated to 30 °C for 20 min after which time the solvent was removed. Dry cyclohexane (5 mL) was added followed by methyl propiolate (4.53 g, 3.2 mL, 54 mmol). The reaction mixture was stirred at room temperature for 20 min after which time the solvent was removed, hot ethanol added, and the resultant mixture refluxed. On cooling, a cream colored precipitate was formed which was collected and washed with ethanol. Analysis of this by NMR in the presence of a standard showed that tetracarbomethoxycyclooctatetraene was formed in 49% yield as a mixture of isomers. ^{1}H NMR of isomer mixture: $\delta =$ 5.65 (m, 4 H), 3.25 (m, 4H).

Representative Procedure for the Nickel-Catalyzed Synthesis of Alkenynes. A small Schlenk tube was charged with nickelocene (38 mg, 0.2 mmol) and $P(O^iPr)_3$ (166 mg, 0.2 mL, 0.8 mmol). After the tube was evacuated under vacuum and filled with nitrogen, the resultant mixture was heated to 80 °C for 10 min after which time dry THF (10 mL) was added followed by allyl acetate (670 mg, 0.72 mL, 6.7 mmol) and phenylacetylene (680 mg, 0.44 mL, 6.7 mmol). The reaction mixture was stirred under reflux for 6 h after which time the mixture was cooled, diluted with THF (30 mL), and filtered and the solvent removed. Analysis of the crude product mixture by NMR in the presence of a standard showed that 5-phenylpent-1-en-4-yne was formed in 78% yield. ^{1}H NMR: $\delta =$ 7.40 (m, 2H), 7.28 (m, 3H), 5.91 (m, 1H), 5.39 (d, 1H), 3.2 (d, 2H).

Acknowledgment. The Royal Society is thanked for a University Research Fellowship. Financial support from King's College London and Hoffmann La Roche is acknowledged.

JO0158377