Nickel Complex-Catalyzed Methyl Ketone Synthesis via Carbonylation of Organic Halides with Tetramethyltin

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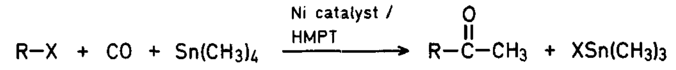
The carbonylation of aryl halides is a useful method for the synthesis of arenecarboxylic acids[1]. However, in order to attain a high catalyst turnover, severe reaction conditions (200–300 °C, 200–300 atm) are normally required. In a previous paper, we reported an unsymmetrical ketone synthesis via a palladium complex-catalyzed carbonylation of halides with organotin compounds[2]. We now found that some nickel complexes also assisted the reaction catalytically under much milder conditions than those used for the synthesis of arenecarboxylic acids from aryl halides.



$$R{-}X + CO + Sn(CH_3)_4 \xrightarrow{\text{Ni catalyst / HMPT}} R{-}\overset{\overset{O}{\|}}{C}{-}CH_3 + XSn(CH_3)_3$$

1 2 3 4

The reaction of iodobenzene with carbon monoxide (20 atm at room temperature) and tetramethyltin in hexamethylphosphoric triamide was run at 120 °C overnight. G.L.C. analysis then showed that acetophenone was formed in 78% yield when $Ni(CO)_2[P(C_6H_5)_3]_2$ was used as a catalyst. Catalytic activity of other nickel complexes was found to be in the order $Ni(CO)_4 < Ni(CO)_3P(C_6H_5)_3 < Ni(CO)_2[P(C_6H_5)_3]_2$, as checked for iodobenzene reactions. $NiCl_2[P(C_6H_5)_3]_2$ also exerted an activity comparable to that of $Ni(CO)_3P(C_6H_5)_3$, while use of $NiCl_2[(C_6H_5)_2PCH_2CH_2CH_2P(C_6H_5)_2]$ afforded only a trace amount of acetophenone. The results obtained with other halides are summarized in the Table.

Although palladium complexes are more active for this reaction, in the case of less reactive halides they gradually decompose to palladium metal as the reaction progresses, while the nickel complexes do not decompose but retain homogenity through and after the reaction. Recently, Rhee and coworkers reported an unsymmetrical diaryl ketone synthesis by the reaction of aryl iodides, arylmercury(II) halides, and nickel carbonyl[3]. However, this reaction is not catalytic but requires a stoichiometric amount of nickel carbonyl which many chemists are, in spite of its versatility in organic syntheses[1,4,5], reluctant to use because of its toxic nature. On the other hand, the present reaction is catalytic, and the catalyst, $Ni(CO)_2[P(C_6H_5)_3]_2$, is air-stable. The major drawback we have to mention is the lack of the reaction with tetraphenyltin under analogous conditions, thus prohibiting unsymmetrical diaryl ketone synthesis.

This reaction may be rationalized by the following scheme:

Table. Methyl Ketones 3 prepared from Halides 1

Product[a] No.	R	Yield [%][b]	Reaction Conditions					m.p. [°C] or b.p. [°C]/torr	
			Catalyst (mmol·10²)	Halide (mmol)	2 (mmol)	Temp. [°C]	Time [h]	found	reported
3a	C_6H_5	28	$Ni(CO)_4$ (5.63)	C_6H_5—J (3.75)	1.88	120°	24		
		37	$Ni(CO)_3P(C_6H_5)_3$ (5.63)	C_6H_5—J (3.75)	1.88	120°	24		
		78 (73)	$Ni(CO)_2[P(C_6H_5)_3]_2$ (5.63)	C_6H_5—J (3.75)	1.88	120°	24	208°/760	202°/760[6]
		59	$NiCl_2[P(C_6H_5)_3]_2$ (5.63)	C_6H_5—J (3.75)	1.88	120°	24		
3b	4-H_3C—C_6H_4	62[c]	$Ni(CO)_2[P(C_6H_5)_3]_2$ (1.88)	4-H_3C—C_6H_4—J (1.88)	2.25	150°	12	—	—
3c	4-H_3CO—C_6H_4	94 (88)[d]	$Ni(CO)_2[P(C_6H_5)_3]_2$ (5.63)	4-H_3CO—C_6H_4—J (1.88)	2.25	140°	24	34.5–36.5°	38–39°[6]
3d	4-C_2H_5OOC—C_6H_4	95 (87)	$Ni(CO)_2[P(C_6H_5)_3]_2$ (5.63)	4-C_2H_5OOC—C_6H_4—J (1.88)	2.25	140°	24	53.1–53.5°	54–56°[7]
3e	2-thienyl	51 (48)[e]	$Ni(CO)_2[P(C_6H_5)_3]_2$ (5.63)	2-C_4H_3S—J (1.88)	2.25	140°	8.5	130°/21	94.5–96.5°/13[6]
3f	4-NC—C_6H_4	41[f]	$Ni(CO)_2[P(C_6H_5)_3]_2$ (5.63)	4-NC—C_6H_4—Br (1.88)	2.25	140°	24	—	—
3g	$C_6H_5CH_2$	29[g]	$Ni(CO)_2[P(C_6H_5)_3]_2$ (5.63)	$C_6H_5CH_2$—Br (1.88)	2.25	150°	0.5	—	—

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[a] Satisfactory microanalyses obtained for **3a, c, d, e** (C ±0.32, H ±0.21).

[b] Determined by G.L.C. analysis and based on the amount of halides or tetramethyltin whichever used in less amount. The figures in parentheses are yields for isolated, pure samples.

[c] Conversion 66.7%.

[d] Conversion 97.5%.

[e] Conversion 63.0%.

[f] Conversion 59.4%. *p*-Toluonitrile was also formed in 8.2% yield.

[g] Dibenzyl ketone (5.2%) and bibenzyl (35.6%) were also formed.

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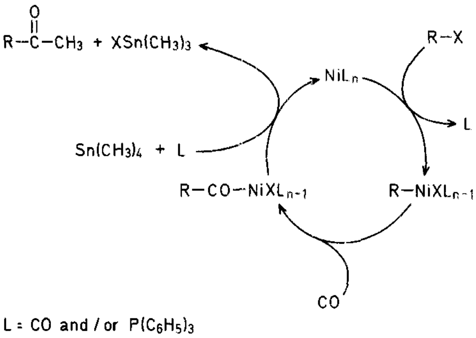

Although the full scope of the present reaction has not been revealed, a wide range of functional groups may, taking the results of carbonylation of aryl halides as well as palladium-catalyzed ketone synthesis into consideration, be tolerated under the reaction conditions.

Carbonylation of Organic Halides 1 with Tetramethyltin (2) and Carbon Monoxide; General Procedure:

An organic halide **1** (3.75 or 1.88 mmol), tetramethyltin (**2**; 337 or 403 mg, 1.88 or 2.25 mmol), the nickel complex catalyst (5.63 or 1.88×10^{-2} mmol), hexamethylphosphoric triamide (1.5 ml), and carbon monoxide (20 atm) are charged into a 27 ml stainless steel autoclave. The mixture is stirred for the period designated in the Table. The resultant mixture is, after G.L.C. analysis (diethylene glycol succinate polyester on Neopak AS, 2 m × 3 mm), poured into ether/water (2:1, 50 ml). The ether layer is washed with water (2 × 10 ml), dried over magnesium sulfate, and concentrated. The residue is purified either by silica gel chromatography with hexane/benzene (gradient) as an eluent (**3a, c, e**) or by recrystallization from hexane (**3d**). Identity of the products was confirmed by comparison of I.R. and ^{1}H-N.M.R. spectra and retention times on G.L.C. analysis with those of authentic samples.

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