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REDUCTIVE COUPLING OF BENZYL HALIDES USING NICKEL(0)-COMPLEX GENERATED *IN SITU* IN THE PRESENCE OF TETRAETHYLAMMONIUM IODIDE, A SIMPLE AND CONVENIENT SYNTHESIS OF BIBENZYLS

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Zerovalent nickel complex generated in situ by reduction of $NiBr_2(PPh_3)_2$ with zinc powder in the presence of Et_4NI was found to be an effective catalyst for homo-coupling of benzyl halides. The catalytic reactions proceeded smoothly in various solvents under mild conditions to afford dehalogenative-coupling products in good to high yields.

It has been shown recently that several zerovalent nickel complexes exhibit specific ability in a reductive coupling of aryl or alkenyl halides.$^{1)}$ In particular, nickel(0)-complexes generated in situ from $NiX_2(PPh_3)_2$ with zinc powder are simple and convenient catalysts for the coupling of aryl halides.$^{2)}$ We have found that the nickel(0)-complex prepared in situ by reduction of $NiX_2(PPh_3)_2$ with zinc in the presence of Et_4NI is an effective catalyst for the homo-coupling of benzyl halides under very mild conditions. Although many methods for the reductive coupling of benzyl halides with metallic nickel or other transition metals are known,$^{3)}$ the method described in this paper provides an alternative way for the synthesis of bibenzyls.

$$ArCH_2X \xrightarrow[\text{rt}]{NiBr_2(PPh_3)_2,\ Zn,\ Et_4NI} ArCH_2CH_2Ar$$

Nickel(0)-complex was simply prepared by stirring a mixture of $NiX_2(PPh_3)_2$ (0.05 equiv.) and Zn (1.5 molar equiv.) in the presence of Et_4NI or LiI (1 equiv.) in various solvents at room temperature for 15 min-1.5 h. The resulting reddish brown mixture was used for the reductive coupling of benzyl chloride or bromide.

The results of the reaction are summarized in Table 1. $NiCl_2(PPh_3)_2$, $NiBr_2(PPh_3)_2$ and $NiI_2(PPh_3)_2$ can be employed as the nickel(II) precursors for the reductive homo-coupling of benzyl chloride (runs 1-3). Benzyl chloride can be converted into bibenzyl in better yield than benzyl bromide (runs 2 and 4). The coupling of benzyl chloride proceeds in various solvents at room temperature within 0.7-2 h when performed in the presence of Et_4NI (runs 5-8). For the reductive coupling, in situ generated $Ni(PPh_3)_4$ can be also used, but the yield of bibenzyl obtained is lower (run 9), and in the absence of Et_4NI and PPh_3, the yield of bibenzyl decreases greatly (run 10). When the reaction is carried out in THF, Et_4NI can be replaced by LiI (run 11). In benzene, however, no coupling reaction occurred in the presence

Table 1. Coupling of benzyl chloride and bromide

Run	Benzyl halide	Conditions		Solv.	Additive	Yield[c)]/%
		Catalyst[a)]	Time/h[b)]			
1	$PhCH_2Cl$	$NiCl_2(PPh_3)_2$	1.5	THF	Et_4NI	94
2	$PhCH_2Cl$	$NiBr_2(PPh_3)_2$	1.5	THF	Et_4NI	95
3	$PhCH_2Cl$	$NiI_2(PPh_3)_2$	1.5	THF	Et_4NI	94
4	$PhCH_2Br$	$NiBr_2(PPh_3)_2$	1.5	THF	Et_4NI	88
5	$PhCH_2Cl$	$NiBr_2(PPh_3)_2$	2	Benzene	Et_4NI	91
6	$PhCH_2Cl$	$NiBr_2(PPh_3)_2$	0.7	CH_3CN	Et_4NI	93
7	$PhCH_2Cl$	$NiBr_2(PPh_3)_2$	1	DMF	Et_4NI	84
8	$PhCH_2Cl$	$NiBr_2(PPh_3)_2$	1.5	Acetone	Et_4NI	96
9	$PhCH_2Cl$	$NiBr_2(PPh_3)_2$	1	DMF	PPh_3[d)]	70
10	$PhCH_2Cl$	$NiBr_2(PPh_3)_2$	5	THF	---[e)]	40
11	$PhCH_2Cl$	$NiBr_2(PPh_3)_2$	1.5	THF	LiI	91
12	$PhCH_2Cl$	$NiBr_2(PPh_3)_2$	3	Benzene	LiI	0[f)]

a) 5 Mol% of $NiX_2(PPh_3)_2$ was used. b) At room temperature. c) Isolated yield of bibenzyl. d) 0.1 Equiv. of PPh_3 was used. e) In the absence of Et_4NI and PPh_3. f) Benzyl chloride was recovered.

of LiI in place of Et_4NI (run 12).

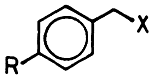
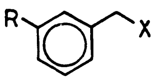
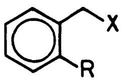
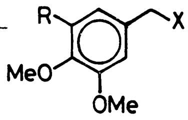
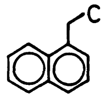
Although it is known that iodide ion present in the system facilitates the nickel-catalyzed homo-coupling,[2b,4)] the use of Et_4NI makes it possible to achieve the reaction in various solvents. Furthermore, the homo-coupling reaction of benzyl halides with nickel(0)-complex in the presence of Et_4NI proceeds smoothly without an additional PPh_3,[5)] and affords bibenzyl alone in high yield, whereas the homo-coupling reaction of benzyl halides with other active nickel-catalysts gives a mixture of coupled product (bibenzyl) and reduction product (toluene).[6)] The addition of PPh_3 and the formation of reduction product frequently cause problems in isolating the coupled product.

The results of the homo-coupling of substituted benzyl halides summarized in Table 2 were obtained under similar reaction conditions mentioned above. The reductive coupling reaction of para- and meta-substituted benzyl halides gave the corresponding bibenzyls in good to high yields except 3- and 4-cyano derivatives (runs 13-17 and 20-23). The benzyl halide having 4-nitro group failed to couple with catalytic amounts of nickel(0)-complex in the presence of Et_4NI and only coupled with equimolar amounts of nickel-complex to give the corresponding bibenzyl in low yield (runs 18 and 19). Ortho-substituted benzyl halides gave also the corresponding bibenzyls in good yields, when treated in benzene (runs 24-28). In contrast to the results in benzene, the reaction of ortho-substituted benzyl halides in THF gave a mixture of homo-coupled products and dehalogenative reduction products. For example, the reaction of 2-bromomethylbenzonitrile (**1**) in THF afforded 1,2-bis-(2-cyanophenyl)ethane (**2**, 40%) and 2-methylbenzonitrile (**3**, 30%), whereas similar reaction in benzene gave simply the coupled product (**2**) and the formation of the reduction product (**3**) was not observed (run 27). More definitive solvent effect was observed in the case of 1-chloromethylnaphthalene. The reaction of 1-chloromethylnaphthalene in THF afforded only the reduction product, 1-methylnaphthalene.

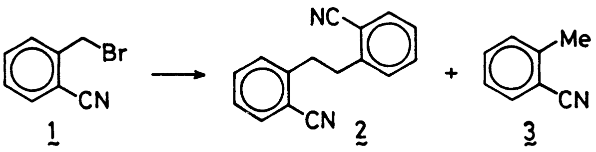
On the other hand, similar reaction in benzene gave the homo-coupled product, 1,2-bis(1-naphthyl)ethane, in good yield as the sole product (run 31). The naturally occurring bibenzyls [brittonin A (**4**)7) and 1,2-bis(3-bromo-4,5-dimethoxy)ethane (**5**)8)] can be prepared in good yields and bromine substituted in benzene ring does not react under these conditions (runs 29 and 30).

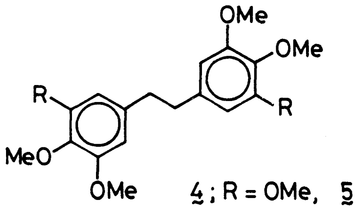
A typical procedure is as follows. A mixture of $NiBr_2(PPh_3)_2$ (0.5 mmol), activated zinc powder (15 mmol), and Et_4NI (10 mmol) was evacuated and flushed with argon. Abs. THF (10 ml) was added and the mixture was stirred at room temperature for 30 min. Benzyl chloride (10 mmol) in abs. THF (5 ml) was added and the resulting mixture was stirred for 1.5 h. Hexane (15 ml) was added, and the precipitate was collected and washed with benzene. The filtrate and washings were evaporated in vacuo and the residue was chromatographed on silica gel to give 867 mg (95% yield) of bibenzyl.

Table 2. Coupling of substituted benzyl halides

Run	Substituted benzyl halide	R	X	Conditions Catalyst a)/mol%	Time b)/h	Solv.	Yield c) %	mp/°C
13		Me	Cl	5	2	THF	96	81.5-82.0
14		OMe	Cl	5	2	THF	89	127.0-128.0
15		Cl	Cl	5	1.5	THF	80	99.5-100.0
16		CN	Br	5	4	Acetone	51	200.0-202.0
17		CO_2Me	Br	5	2.5	THF	82	50.0-50.5
18		NO_2	Br	5	1.5	THF	0 d)	
19		NO_2	Br	100	2	THF	28	181.5-183.0
20		Me	Br	5	2	THF	85	—— e)
21		OMe	Br	5	2	THF	79	—— e)
22		CN	Br	5	3	THF	55	160.5-161.0
23		CO_2Me	Br	5	2	THF	75	84.5-86.5
24		Me	Cl	10	2	Benzene	89	64.0-65.5
25		OMe	Br	10	4	Benzene	87	84.0-84.5
26		Cl	Cl	5	3	THF	71	56.5-58.5
27		CN	Br	10	2.5	Benzene	71	142.0-142.5
28		CO_2Me	Br	10	2.5	Benzene	65	101.0-102.5
29		OMe	Br	10	2	THF	70	138.5-139.0
30		Br	Cl	10	2	THF	73	148.0-148.5
31				10	2	Benzene	74	163.0-163.5

a) $NiBr_2(PPh_3)_2$ was used for the preparation of the nickel(0)-complex. b) At room temperature. c) Isolated yields of substituted bibenzyls. d) Starting material was recovered. e) Colorless oil.





4; R = OMe, **5**; R = Br

As mentioned above, the reductive homo-coupling reaction of benzyl and substituted benzyl halides with the nickel(0)-complex and Et_4NI proceeds under mild conditions to afford bibenzyls in good to high yields. Although we examined the homo-coupling reaction of 4-methoxy-, 4-cyano-, and 2-methylbenzyl halides, and 1-chloromethylnaphthalene with in situ generated $Ni(PPh_3)_4$ in DMF or THF, the yields of the corresponding bibenzyls were low and considerable amounts of the dehalogenative reduction products were obtained. The nickel(0)-complex generated by reducing $NiBr_2(PPh_3)_2$ in the presence of Et_4NI may be plausibly recognized as $Ni(PPh_3)_2$ which could not be prepared previously.$^{9)}$ Recently, Takagi has reported the homo-coupling reaction of aryl and vinyl halides using $Ni(PEt_3)_2$ and KI in HMPA; however, the use of $Ni(PPh_3)_2$ and KI gave poor results.$^{5)}$ It is worth noting that the bis-ligand nickel(0)-complexes can be generated in situ and employed for the homo-coupling reactions always in the presence of iodide ion, hence a nickel(0)-complex containing iodide ion [e.g., $Ni(PPh_3)_2(I^-)$] may play an important role in these reactions.$^{10,11)}$ Further investigation elucidating the active species is now in progress.

References

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10) Casser has reported iodotricarbonylnickel(0) anion $[INi(CO)_3]^-$ as the active species in the carbonylation of benzyl halides. See, L. Casser, G. P. Chiusoli, and F. Guerrieri, Synthesis, 1973, 509.

11) The electronic spectrum of the nickel(0)-complex [a possible structure is $[INi(PPh_3)_2]^-$] generated in situ in the presence of Et_4NI in benzene shows the absorption maximum at 426 nm, which is different from that of $Ni(PPh_3)_3$ in benzene (λ_{max} 393 nm).$^{9)}$

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