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REGULAR ARTICLE

Ni(II)/Al(0) mediated benzylic Csp^3-Csp^3 coupling in aqueous media

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Abstract. The reaction of benzyl bromides and chlorides with aluminium metal powder or foil (1.2 eqv.) in the presence of catalytic nickel nitrate (10 mol%) in water at room temperature resulted in homocoupling to the corresponding bibenzyl products which were isolated in moderate to good yields. In sharp contrast, the same reaction in organic solvents like dichloromethane, dimethylformamide, acetonitrile, methanol and toluene yielded only a trace amount of the desired product. The scope of the reaction was tested with substituents on the aromatic ring such as Me-, Cl-, CN-, F-, NO_2-, Ph- as well as 2° benzyl halides.

Keywords. C-C bond formation; reaction in water; aluminium; nickel; benzyl halide.

1. Introduction

Carbon-carbon bond formation *via* coupling reactions is one of the most fundamental transformations in organic synthesis.[1] The well-known oxidative addition–transmetallation– reductive elimination sequence is in the textbook premise. On a relative scale, coupling reactions involving organometallic partner bearing sp and sp^2 hybridized carbons[2] outwits those having sp^3-hybridized carbon centers.[3] In this regard we were drawn to the Csp^3-Csp^3 homocoupling of benzylic halides leading to bibenzyl derivatives, the latter being key building blocks for the synthesis of dyes, polymers, agrochemicals and pharmaceuticals.[4] Although Wurtz coupling is historically the first in alkyl and aryl homocoupling,[5] the post-Wurtz era showed the advent of many reagents for benzylic homocoupling which include either a metal or the dual reagent combination of a metal and a catalytic transition metal partner.[6] Also interesting are the examples of benzylic homocoupling in aqueous medium[7] which are of relevance in the context of green chemistry.

Although aluminium metal has similar electronegativity as zinc, examples of benzylic activation by aluminium metal is lesser explored. The work of Knochel and co-workers on the generation of benzylic aluminum sesquichlorides from corresponding benzyl halide and aluminum powder in the presence of catalytic In(III) halide in THF is worthy of mention here.[8] The benzyl aluminum reagents were transmetallated to the corresponding benzyl zinc reagents and subsequently used for coupling reactions.

In this manuscript, we demonstrate a highly facile homocoupling of benzyl bromide to the corresponding bibenzyl in the presence of aluminum powder (1.2 eqv.) and catalytic Ni(II) salt in water at room temperature. To our knowledge, this is the first example of the use of aluminum metal in C-C coupling in water and adds to its green relevance. Studies on the effect of solvent clearly showed the superiority of water over a host of other organic solvents.

2. Experimental

2.1 *General procedure for the homo-coupling of benzyl halides*

To a suspension of aluminium powder (1.2 eq) in water (5 mL), $Ni(NO_3)_2.6H_2O$ (10 mol%) was added and the reaction

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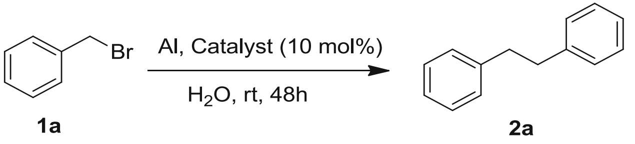
mixture was degassed using argon. The suspension was stirred at room temperature for 5 min. Benzyl halide (3 mmol) was added slowly to the reaction mixture, and the mixture was stirred at room temperature for 48 h under argon. The mixture slowly turned into a clear solution and the bibenzyl crystals were seen to be floating on top of the solution. The mixture was quenched with hydrochloric acid (4M, 5 mL) and extracted with dichloromethane. The combined organic extract was washed with water and dried over Na_2SO_4. The solvent was removed and the residue was purified by chromatography or recrystallization. All products gave satisfactory spectroscopic data and were compared with authentic sample wherever available.

3. Results and Discussion

In the initial screening, we tested the reaction of benzyl bromide **1a** with various metals in water at room temperature under argon atmosphere. In the case of Sn, Zn and Al metals, bibenzyl **2a** was obtained in 35, 47 and 58% yields respectively. Next, we explored the reaction of **1a** in the presence of aluminium metal (1.2 eqv.) and a catalytic 3d-transition metal salt (Table 1). In the absence of a catalyst, the yield of **2a** was 58% (Table 1, entry 1). As catalyst $FeCl_3$ and $CoCl_2$ could not improve the yield (entries 8, 9). On the other hand, water-soluble Ni(II) salts showed significant catalytic effect (entries 2, 4–7). Among various nickel salts, $Ni(NO_3)_2.6H_2O$ was found to be most efficient. After 48 h, the reaction mixture became fully transparent with crystals of **2a** floating on top; the latter was isolated in 82% yield (Table 1, entry 6). A similar reaction but with aluminium foil yielded **2a** in 65% yield (entry 7).

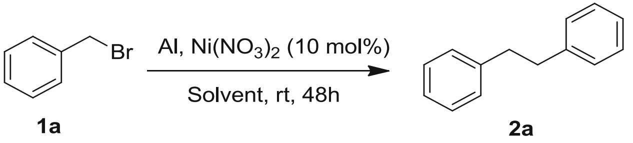
Table 1. Homo-coupling of benzyl bromide using Al(0)/transition metal salts in water.[a]



Entry	Catalyst	Yield of **2a** (%)[b]
1	nil	58
2	$NiCl_2.6H_2O$	70
3	$NiCl_2(PPh_3)_2$	57
4	$NiBr_2$	62
5	$Ni(acac)_2$	70
6	$Ni(NO_3)_2.6H_2O$	82
7	$Ni(NO_3)_2.6H_2O$	65[c]
8	$CoCl_2$	60
9	$FeCl_3$	50

[a] **1a** (3 mmol), Al (1.2 eqv.), water (5 mL), room temperature. [b] refers to isolated yield of pure product after chromatography/crystallization. [c] aluminium powder was replaced by finely cut pieces from an aluminium foil.

Table 2. Homo-coupling of benzyl bromide using Ni(II)/Al(0): Effect of solvents.[a]



Entry	Solvent	Yield of **2a** (%)[b]
1	DCM	< 5
2	DMF	< 5
3	Toluene	Nil
4	Acetonitrile	Nil
5	Methanol	< 5
6	H_2O	82

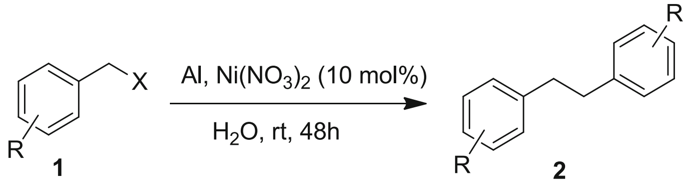
[a] **1a** (3 mmol), Al (1.2 eqv.), solvent (5 mL), room temperature. [b] refers to isolated yield of pure product after chromatography/crystallization.

The *water-effect*[9] in the present reaction became glaring when we studied the reaction in various organic solvents (Table 2). None of the solvents tried, including polar protic, polar aprotic, as well as non-polar solvents, could facilitate the reaction in a manner that water did. Trace amounts of the product were detected for reactions in methanol, DMF and DCM. As stated earlier, in water, the mixture turned in to a clear solution on completion of the reaction. The clear solution showed a pH value between 6–7 (pH paper).

A recent paper on the reductive coupling of benzyl halides using catalytic Ni(0)-on-alumina in the presence of hydrazine hydrate as co-reductant is noteworthy.[7b] Encouraged by this report we attempted the reaction of **1a** (3 mmol) with 80% hydrazine hydrate (2 mL) in water. The colour of the mixture instantly changed from green to pink. Even after 48 h, there was no conversion of **1a**, which was isolated back in quantitative yield.

The scope of the present reaction was tested with various substituted benzyl bromide and benzyl chlorides **1a**–**1n** using aluminum powder (1.2 eqv.) and nickel nitrate hexahydrate (10 mol %) as a catalyst in aqueous medium and at room temperature (Table 3). The following results are noteworthy. Benzyl bromides were more reactive than benzyl chlorides, while aryl halides were completely non-reactive (entries 1–3, 7, 10–12, 14, 15–17). Secondary benzyl halides were also amenable to the reaction (entries 8, 9). Both electrons donating (entries 2, 3, 12, 13) and withdrawing (entries 4–7, 14) substituent on the benzene ring were tolerated. The attempted reaction between benzyl bromide and bromobenzene in the presence of Ni(II)/Al did not result in the formation of diphenyl methane as the cross-coupled product.

Table 3. Homo-coupling of benzyl bromide using Ni(II)/Al(0): Substrate Scope.[a]



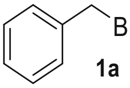
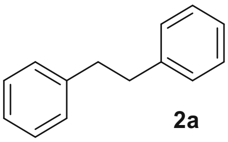
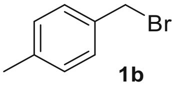
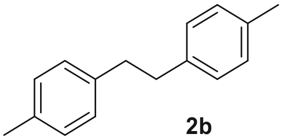
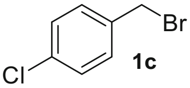
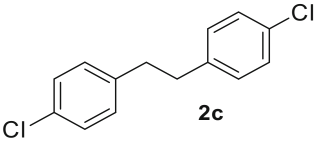
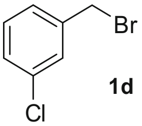
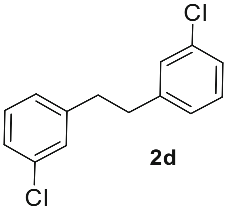
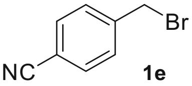
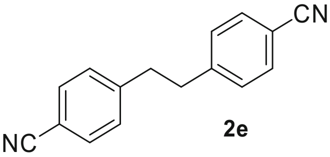
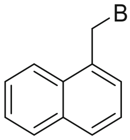
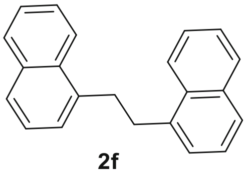
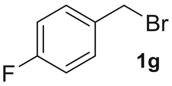
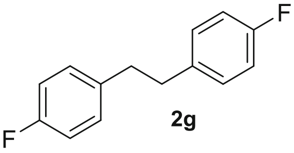
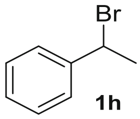
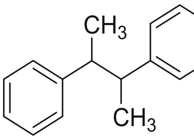
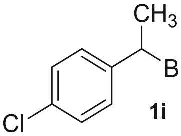
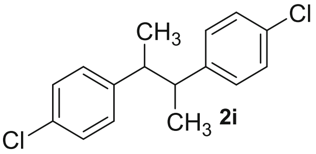
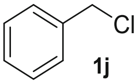
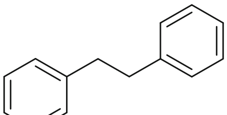
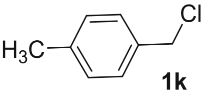
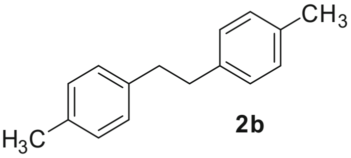
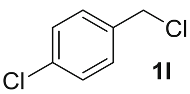
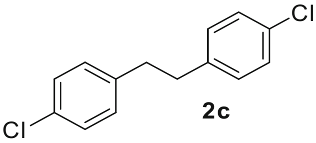
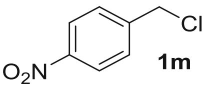
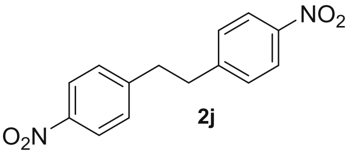
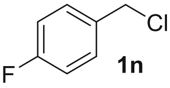
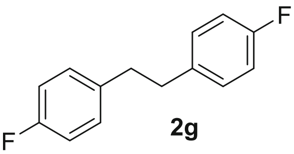
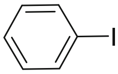
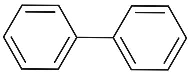
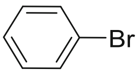
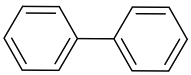
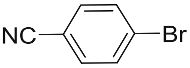
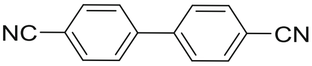
Entry	Substrate	Product	Yield of **2** (%)[b]
1	 **1a**	 **2a**	82
2	 **1b**	 **2b**	90
3	 **1c**	 **2c**	70
4	 **1d**	 **2d**	68
5	 **1e**	 **2e**	60
6	 **1f**	 **2f**	68
7	 **1g**	 **2g**	62

Table 3. (*contd.*)

8	 **1h**	 **2h**	26
9	 **1i**	 **2i**	71
10	 **1j**	 **2a**	24
11	 **1k**	 **2b**	40
12	 **1l**	 **2c**	5
13	 **1m**	 **2j**	nil
14	 **1n**	 **2g**	10
15	 **1o**	 **2k**	nil
16	 **1p**	 **2k**	nil
17	 **1q**	 **2l**	nil

[a] **1** (3 mmol), Al (1.2 eqv.), water (5 mL), room temperature. [b] refers to isolated yield of pure product after chromatography/crystallization.

3.1 ^{1}*H NMR monitoring of reaction mixture*

The reaction of aluminium metal with benzyl bromide in water being novel, we explored the reaction by ^{1}H NMR in D_2O as solvent (Supplementary Information). A mixture of aluminium powder (96 mg, 3.6 mmol) and benzyl bromide (3 mmol) in D_2O (4 mL) was stirred. After 24 h, the mixture was separated into two parts. In one part, $CDCl_3$ was added and the organic phase was subjected to NMR analysis (Figure S1a, Supplementary Information,). The other part in D_2O was directly checked for NMR using tert-butanol as internal standard (Figure S1b, Supplementary Information,). The organic phase showed the presence of bibenzyl and unreacted benzyl bromide. The aqueous phase indicated the formation of a new product with methylene proton at 1.88 ppm, and phenyl proton at 6.9–7.1 ppm indicating the presence of a benzyl group in the product.[10] Attempts to run ESI-MS of the solution is in progress.

4. Conclusions

In conclusion, we have demonstrated a simple and practical method for homocoupling of benzyl halides using aluminium powder and nickel nitrate as a catalyst under mild conditions in an aqueous medium. Further work in extending the scope of the reaction is in progress.

Supplementary Information (SI)

General methods, spectral data and figures are available at www.ias.ac.in/chemsci.

Acknowledgements

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