

Heterogeneous Rh/C-Catalyzed Direct Reductive Coupling of Haloaryls to Biaryls in Water

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Abstract:

Reductive coupling of haloaryls and substituted haloaryls to the respective biaryls is effected in water with good selectivity, using a reducing agent such as formate salts and a base, NaOH, in the presence of a catalytic amount of PEG-400 and 5% Rh/C catalyst at 115 °C temperature. The catalyst can be recycled. The competing reduction reaction is minimized with proper alteration of the operating conditions. The role of temperature, catalyst loading, reducing agents, base, and PEG-400 are discussed. The reaction follows a zero-order kinetics.

Introduction

The syntheses and utilization of biaryl compounds is a subject of considerable contemporary interest as they represent important building blocks for numerous agrochemicals, pharmaceuticals, and a large number of natural products of varied structure, biological activity, and biosynthetic origins. Also, biaryls are the structural units of the chiral skeleton of many of the asymmetric catalysts.¹ In addition to the stoichiometric classic general Ullmann,² Suzuki,³ and Stille⁴ coupling reactions, Pd-catalyzed reductive coupling of haloaryls have gained the attention of many researchers as this process benefits from simple reactor design, easy catalyst separation, and recycling.⁵ We have recently demonstrated success in Pd-catalyzed reductive coupling^{6a–d} of haloaryls in water, using a variety of reductants in the presence of a catalytic amount of phase-transfer agent. Use of hydrogen gas as the reducing agent in water enhances the economic viability of these Pd-catalyzed processes;^{6b} however, the formation of side products (25–35%), derived from the concurrent hydrodehalogenation reactions⁷ of haloaryls to

arenes restricts the usage of this process for a commercial-production scale. While side reactions can be minimized, the implementation of this system becomes uneconomical as a mixture of expensive catalysts⁸ and toxic solvents⁹ is required. The use of expensive starting materials such as haloaryls has been avoided by using benzene as the starting material in the oxidative coupling reaction;¹⁰ however, this necessitates the use of high pressure and a mixture of homogeneous catalysts including PdCl₂, which may not be reusable.

Therefore, there is an incentive to search for different heterogeneous catalysts for reductive coupling reactions. In fact, homogeneous Rh salts have previously been used for biaryl synthesis from arylmercuric complexes,¹¹ and recently, these have also been used for the borylation of aromatic and benzylic C–H bonds.¹² As part of our continuing search for a catalytic process for synthesizing biaryls, we present in this communication results on the Rh/C-catalyzed reductive coupling of haloaryls to biaryls in water. These reactions are the first direct Rh-catalyzed reductive coupling of haloaryls to form biaryls and were carried out at 115 °C in water with formate salts as the in situ catalyst regenerator.

Results and Discussion

In a typical reaction¹³ (see Experimental Section), a 300-mL high-pressure autoclave was charged with halobenzene, sodium hydroxide, sodium formate, water, and catalytic amounts of PEG-400 and 5% Rh/C catalyst. After 18–23 h at 115 °C, depending on reaction conditions, biphenyl and benzene (ArH) were the major products. Good to moderate yields of the coupling products (Ar–Ar) were obtained using various substrates.

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Table 1. Rh/C-catalyzed reductive coupling of haloaryls^a

entry	haloaryl	% conversion	% selectivity, coupling	% selectivity, reduction
1	ArI ^b	89	56	44
2	ArBr	73	49	51
3	ArCl ^c	61	36	64
4	CT ^d	59	21	68
5	CT ^e	59	14	81
6	CTT ^f	69	28	67
7	CA ^g	23	6	94
8	CP ^h	32	12	88
9	CBA ⁱ	27	8	92
10	BN ^j	10	6	94

^a Reaction conditions: starting material, 0.044 mol; sodium formate, 4.76 g (0.07 mol); sodium hydroxide, 5 g (0.125 mol); 5% Rh/C, 1.0 g (1.1 mol %); PEG-400, 1.5 g (8.5 mol %); temperature, 115 °C, solvent, water (total volume) 50 mL; reaction time, 20 h. ^b 18 h. ^c 23 h. ^d 4-Chlorotoluene. ^e 2-Chlorotoluene. ^f 4-Chloro-1,1,1-trifluorotoluene. ^g 4-Chloroanisole. ^h 4-Chlorophenol. ⁱ 4-Chlorobenzoic acid. ^j 2-Bromonaphthalene.

Table 1, entries 1–10, shows the reactivities of different starting materials to form the coupling products. Iodobenzene and bromobenzene are highly reactive to the coupling reaction. Chlorobenzene is moderately reactive. Chlorotoluenes are less reactive than bromobenzene. 4-Chloroanisole, 4-chlorophenol, and 4-chlorobenzoic acid react minimally. Bromonaphthalene is least reactive. The reaction did not go to completion for any of the halobenzenes used. For example, with bromobenzene, 73% conversion was achieved after 20 h. For the determination of kinetics and suitable process parameters, bromobenzene was used as a model substrate.

The temperature plays a significant role on both the rate of reaction and the selectivity to biphenyl. In particular, an increase in temperature of the reaction shifted the selectivity towards coupling (Table 2, entries 1–4). This may be due to $E_{a,coupling} > E_{a,reduction}$,^{6b,14} however, at 125 °C, we observed the formation of diphenyl ether (9%) in addition to the biphenyl and benzene. This side product may be the result of halo-substitution by OH⁻ at the higher temperature. Also, the general trend indicates that at higher Rh/C catalyst loadings, the faster is the reaction. At low catalyst loadings, there was a direct correlation between catalyst loading and selectivity. However when the catalyst loading exceeded 1.1 mol %, no further increase in selectivity was observed (Table 2, entries 5–8). Conversely, addition of sodium hydroxide⁷ shifted the product distribution towards the coupling product from 11 to 49%. Moreover, the addition of 0.125 mol NaOH optimized the selectivity as well as the rate of reaction (Table 2, entries 9–11). In addition, further increases in these two parameters were observed when formate was added, the selectivity shifted towards the reduction product when formate concentration exceeded 0.07 mol (Table 2, entries 12–15). Here, all subsequent reactions were performed with 0.07 mol formate concentration to attain a maximum selectivity of 49% to biphenyl.

With an increase in PEG-400 concentration from 0 to 8.5 mol % of the substrate, the rate of reaction increased marginally (Table 2, entries 16–18). However, at higher

Table 2. Effect of different process parameters on the coupling reaction^a

entry	parameter	% conversion	% selectivity, Ar–Ar	% selectivity, Ar–H
1	temp, 95 °C	21	33	67
2	105 °C	43	41	59
3	115 °C	73	49	51
4	125 °C	92	52	39
5	5% Rh/C, 0.75 mol %	40	37	63
6	1.1 mol %	73	49	51
7	1.5 mol %	74	48	52
8	2.0 mol %	74	50	50
9	NaOH, 0 mol	47	11	89
10	0.125 mol	73	49	51
11	0.2 mol	74	50	50
12 ^b	formate, 0 mol	0	0	0
13	0.05 mol	64	48	52
14	0.07 mol	73	49	51
15	0.09 mol	74	37	63
16	PEG-400, 0 mol %	49	34	66
17	8.5 mol %	73	49	51
18	11 mol %	76	31	69

^a Reaction conditions: bromobenzene, 6.9 g (0.044 mol); sodium hydroxide, 5 g (0.125 mol); PEG-400, 1.5 g (8.5 mol %); temperature, 115 °C, solvent, water (total volume) 50 mL; reaction time, 20 h; ^b reaction time was 10 h.

PEG-400 loadings, the yield was reduced due to competition from a reductive side reaction of bromobenzene to benzene. Presumably this is due to the hydrogen-donating nature of PEG-400. While, PEG-400 does not alter the chemical nature of the intermediates, it may modify the physical micro-environment around the catalyst surface.¹⁵

Different reducing agents were also examined to optimize the process. With H₂ gas, reduction was much faster, and a 95% conversion was achieved in 10 h; however, the selectivity to biphenyl was unexpectedly lower (33%) than that of formate salts (49%).

The solid Rh/C catalyst could be recycled simply by filtering and then suspending the solid in methanol–water with stirring under 5 atm hydrogen pressure at 60 °C for 5 h. The same catalyst retained its activity when tested up to five reuses. For an easy separation of the catalyst, a biphasic reaction media (1:1 mixture of water and toluene) could be used for this reaction; however, the conversion and selectivity remained the same when bromobenzene was used as the substrate.

We previously proposed a mechanism^{6a} for the Pd-catalyzed coupling of chloroaryls which consists of two single-electron-transfer (SET) processes from the Pd⁰ to two chlorobenzene molecules,¹⁶ followed by dissociation of the [Ar–Cl]^{•-} radical anions. Similarly, the oxidized form of Rh could be either Rh¹⁺ or Rh³⁺ unlike the Pd which is converted to Pd²⁺. The hydrogen generated from formate in the presence of Rh⁰ could reduce Rh¹⁺ or Rh³⁺ back to Rh⁰, and ultimately completing the catalytic cycle. While there

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is experimental evidence to support the ability of Rh⁰ to form hydrides¹⁷ and reduce chlorobenzene to benzene the mechanism is not yet known.

The reaction using bromobenzene was also used to study the reaction kinetics. Reaction rates were found to be independent of bromobenzene concentration up to 52% conversion of bromobenzene. The rate equation can be expressed by eq 1

$$-dC_A/dt = k$$

or $C_{A0} - C_A = kt$

or $X_A = k_{\text{obs}}t$ where $k_{\text{obs}} = k/C_{A0}$ (1)

The k values are found to be 0.0345, 0.072, 0.1256, and 0.1494 mol/min at 95, 105, 115, and 125 °C, respectively. Thus, the experimental Arrhenius energy of activation is found to be $E_{\text{act, total}} = 60 \text{ kJ mol}^{-1}$ (14.5 kcal mol⁻¹, $r^2 = 0.9483$ for four measurements at 95, 105, 115, and 125 °C). However, a shift of reaction order from zero- to first-order was observed at higher conversion level (>52%). This may be the reason for incomplete conversion of the starting materials under the reaction conditions. To verify this we added 0.022 mol of a fresh batch of bromobenzene to the same reaction mixture after obtaining 52% conversion on the initial bromobenzene loading. It was observed that the reaction had proceeded again up to 52% conversion level with zero-order kinetics. This rules out the possibility of catalyst poisoning.

Conclusions

Biphenyl was synthesized by the reductive homocoupling of aryl halides in the presence of a phase-transfer catalyst, PEG-400, and a base, at 115 °C in water. Conversion into biphenyl as high as 50% was observed. Furthermore, reaction conditions were optimized to minimize the occurrence of the competing hydrodehalogenation reactions. Our results demonstrate the promise of designing a highly chemoselective Rh catalyst. For example, a systematic ligand design could be used to optimize the coupling of specific substrates, for example, 4-chlorobenzaldehyde or dichlorobenzene.

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Experimental Section

Melting points were measured in glass capillaries using an Electrothermal 9100 instrument. ¹H NMR spectra were measured on a Bruker AMX 300 instrument at 300.13 MHz. GC and GC/MS analyses were performed using an HP-5890 gas chromatograph with a 50% diphenyl–50% dimethylpolysiloxane packed column (25 m/0.53 mm). Chemicals were purchased from commercial firms (>99% pure) and used without further purification. Products were either isolated and identified by comparison of their ¹H NMR spectra to standard samples, or identified by MS data and comparison of their GC retention times with previously isolated reference samples in our laboratory. Reactions were performed in a 300-mL high-pressure Parr autoclave fitted with a six-bladed impeller, a pressure transducer, and a condenser.

General Procedure for Coupling of Haloaryls. *Example: Biphenyl from C₆H₅Br.* Into a 300-mL autoclave fitted with a six-bladed impeller and a cooling coil, were charged 6.9 g (44 mmol) of C₆H₅Br, 4.8 g (70 mmol) of HCOONa, 5.0 g (125 mmol) of NaOH, 1.5 g (8.5 mol %) of PEG-400, 1.0 g of 5% w/w Rh/C (1.1 mol % Rh relative to C₆H₅Br), and water (total reaction volume 50 mL). The reactor was heated to 115 °C, and the reaction progress was monitored by a GC. The mixture was stirred (900 rpm) at 115 °C for 20 h and then cooled to 45 °C. After removing the catalyst by hot filtration at 45 °C, water was added to the filtrate, and the organic compounds were extracted with (4 × 40 mL) CH₂Cl₂. Solvent evaporation and recrystallization afforded 46 mol % (based on C₆H₅Br) of biphenyl, mp 69 °C (from cold EtOH).

Catalyst Recycle. The solid Rh/C catalyst was recycled without losing any catalytic activity by simply washing with water, filtering the solid off, and stirring it in 70–30 methanol–water mixture at 60 °C for 5 h under 5 atm H₂ pressure. After filtration and drying, the same Rh/C retained almost the same catalytic activity as that in the reusability experiments.

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