



# Supported phase-transfer catalysts as selective agents in biphenyl synthesis from haloaryls

Sudip Mukhopadhyay,<sup>a,†</sup> Gadi Rothenberg,<sup>b,‡</sup> Nida Qafisheh<sup>c</sup> and Yoel Sasson<sup>c,\*</sup>

<sup>a</sup>Chemical Engineering Department, University of California at Berkeley, Berkeley, CA 94720, USA

<sup>b</sup>York Green Chemistry Group, Chemistry Department, The University of York, Heslington, York YO10 5DD, UK

<sup>c</sup>Casali Institute of Applied Chemistry, Hebrew University of Jerusalem, Jerusalem 91904, Israel

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**Abstract**—Coupling of substituted halobenzenes to the respective biphenyls is effected with high selectivity in toluene, using a combination of a reducing agent and a weak base in the presence of catalytic tetrabutylammonium bromide (TBAB) and palladium that are both supported on carbon. The maximum selectivity to biphenyl was achieved when Pd, Na<sub>2</sub>CO<sub>3</sub>, and TBAB were all supported together on activated carbon. The results are explained with postulation of a physical micro-membrane formed in situ by the phase-transfer catalyst. © 2001 Elsevier Science Ltd. All rights reserved.

The selective reductive coupling reaction<sup>1</sup> of haloaryls to biphenyls is of major interest to process chemists as these products are important building blocks for numerous agrochemicals and pharmaceuticals.<sup>2</sup> Unfortunately, selectivity is generally low due to the parallel reduction reaction.<sup>3,4</sup> However, the reductive coupling of haloaryls benefits from simple reactor design and easy catalyst separation and recycling. We have recently demonstrated the reductive coupling of haloaryls in water by using formate salts,<sup>5</sup> hydrogen gas,<sup>6</sup> and/or zinc powder<sup>7</sup> as the reducing agent in the presence of a base and catalytic amounts of a phase-transfer catalyst (PTC).<sup>8,9</sup> Our goal was to minimize the reduction side reaction in order to increase the selectivity to biphenyl. Although the effects of PTC on this reaction have been reported over 25 years ago, the function of the PTC in this system is still unclear. Recently, Tundo and co-workers reported<sup>10</sup> the Pt/C-catalyzed hydrodehalogenation of halogenated aryl ketones in presence of PTC. It was proposed that the PTC may adsorb on the catalyst and *embody* it, thus changing the micro-environment in the vicinity of the Pd catalyst. This hypothesis may further our understanding of the role of PTC in similar type of reactions. In applying this concept to our model Pd-catalyzed coupling system, we first tried to understand the difference between a PTC in solution and a supported one. Surprisingly, the supported sys-

tem turned to be most effective, achieving very high yields to biphenyl. Here, we present the results and discuss how the PTC distribution over the porous carbon support could turn the reaction chemoselectively towards the coupling side.

In a typical reaction,<sup>11</sup> the halobenzene and the reducing agent were stirred in the presence of the catalyst and a base to give biphenyl as the major product, together with minor amounts of benzene (the by-product due to the parallel reduction reaction). No other products were observed. Conversions and product selectivities for various halobenzenes are shown in Table 1.

Carbon was the obvious support of choice due to its high surface area and porosity, plus of course its high selectivity as a support in previous Pd-catalyzed reductive coupling studies. Using carbon-supported PTC,<sup>12</sup>

**Table 1.** Coupling reaction with different starting material<sup>a</sup>

Substrate	Time (h)	Conv. (%)	Ar–Ar	ArH
Chlorobenzene	8.5	100	83	17
Bromobenzene	8	100	92	8
Iodobenzene	6	100	93	7

<sup>a</sup> Reaction conditions: Substrate, 16 mmol; support 3 (see Ref. 12), HCOONa, 19 mmol, temperature, 110°C; agitation speed, 900 rpm; solvent, PhMe (total volume 50 mL).

\* Corresponding author. Fax (+972) 2 6528250; e-mail: ysasson@vms.huji.ac.il

† E-mail: sudip@uclink2.berkeley.edu

‡ E-mail: gr8@york.ac.uk

an increased product selectivity was observed (cf. Table 2, entries 1–3).

When  $\text{Na}_2\text{CO}_3$ , TBAB, and Pd were all together supported on carbon, the rate and selectivity obtained were very high under the reaction conditions (Table 2, entries 4 and 5), while depositing the formate on the carbon support together with the other components resulted in a low selectivity to biphenyl due to an increase in reduction rate (Table 2, entry 6).

The amount of water present turned out to be most crucial parameter for this reaction. It has been shown elsewhere<sup>3</sup> that water molecules should also be adsorbed on the Pd surface and will generate hydrogen from reaction with formate salt. In all the reactions, 0.15 g of water was added to get a faster rate and maximum selectivity. When the water amount was further increased to 0.75 g, the selectivity decreased abruptly due to the leaching of PTC from the support. A separate set of experiments has been performed to elucidate the effect of water on the leaching time of PTC from the surface. It was observed that when the water amount was >0.5 g, the leaching had started. However, at a water amount of 3 g, 67% of the PTC was leached out from the surface in 1 h. Thus, the water amount used in all our experiments (0.15 g) is within the safe limit with regard to leaching.

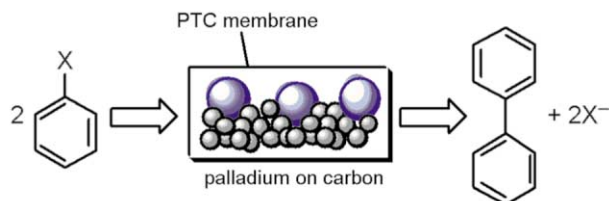
The solid Pd/C catalyst was recycled without losing any catalytic activity by simply stirring it with hot water, followed by filtration and washing with methanol. The same carbon support and Pd were then used to support a fresh batch of PTC, which retained almost the same catalytic activity in the reusability experiments.

**Table 2.** Coupling reaction with different starting material<sup>a</sup>

Entry	Support	Time (h)	Conv. (%)	Select. (%) Ar–Ar
1 <sup>b</sup>	Support 1	6	100	34
2	Support 2	6.5	100	79
3	Support 2A	6	100	75
4	Support 3	8	100	92
5	Support 3A	7.5	100	89
6	Support 4	4	100	56

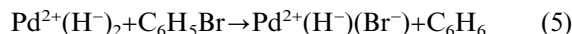
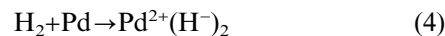
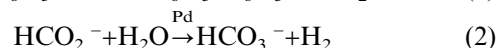
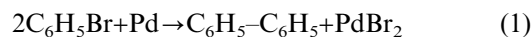
<sup>a</sup> Reaction conditions: Bromobenzene, 2.5 g (16 mmol),  $\text{Na}_2\text{CO}_3$ , 2.5 g (24 mmol), sodium formate, 1.3 g (19 mmol), solvent, PhMe (total reaction volume 50 mL), temperature, 110°C.

<sup>b</sup> TBAB, 0.2 g (0.6 mmol).



**Figure 1.** Cartoon of the PTC membrane hypothesis.

The basic reactions in this reductive coupling system are depicted by Eqs. (1)–(5).



The main difference between the reductive coupling and the reduction is that the homocoupling requires only electrons, while the reduction requires hydrogen atoms. As has been shown before,<sup>5,13</sup> the selectivity to the coupling products depends on the number of vacant active Pd(0) sites, which in turn reflects the balance between the reduction of Pd(II) (Eq. (3)), and the formation of  $\text{Pd}(\text{II})(\text{H}^-)_2$  via Eq. (4). The latter reaction is a function of the available dihydrogen concentration close to the active catalyst surface. From the results of the present study, it appears that the reactions shown in Eqs. (4) and (5) are somehow suppressed to give a higher selectivity to biphenyl. This could be due to the formation of a physical PTC micro-membrane in the vicinity of Pd which can allow the passing of electrons but restricts the hydride formation rate by limiting the formate adsorption on the surface.<sup>10</sup> The marked increase in reaction time (from 6 to 8 h) when compared to the usual solution PTC reaction may indicate such adsorption limitations on the catalyst surface in its surface modified form. The low selectivity to biphenyl that was obtained when using the formate salt on the support clearly points out the fact that there was some extra resistance created on the Pd surface for the solution formate to get adsorbed when formate was administered in solution, thus limiting the effective hydride concentration. Moreover, when the components are supported on the carbon, there is a chance of adsorption of a fractional portion of PTC on the Pd surface during the catalyst preparation and prior to the reaction. The adsorbed PTC species could form a micro-membrane around the Pd catalyst (Fig. 1). However, to form a PTC membrane more effectively, the PTC should be present in close proximity with the solid Pd catalyst, i.e. the PTC should be adsorbed on the Pd surface prior to the reaction. In our opinion, that might be the crucial deciding factor in terms of selectivity. To establish this concept, we performed a reaction similar to that in Table 2 (entry 1) where the PTC and the support 1 were stirred in toluene for 3 h prior to the addition of bromobenzene and formate salt. After the stipulated 6 h reaction period, 52% selectivity to the biphenyl was observed. The increase in product selectivity from 34 to 52% could be due to the formation of the PTC membrane prior to the reaction which provides an extra resistance gradient to the incoming formate molecules from the solution to the Pd surface and thus limiting the hydride formation.

To determine if there were any chemical changes occurring on the surface of the Pd, IR and XRD were performed on the catalyst before and after reaction.

Similar patterns were obtained in each case, supporting our hypothesis that this is a physical adsorption phenomena. Moreover, the catalyst retained its activity when re-used, and the same product selectivity was obtained, irrespective of the reducing agent employed (e.g. with molecular hydrogen, 82% selectivity to biphenyl was achieved).

In conclusion, supporting the PTC on activated carbon can minimize the occurrence of hydrodehalogenation. This permits the usage of a weak base, such as  $\text{Na}_2\text{CO}_3$ , thus making this process attractive from the standpoint of cost and waste-disposal concerns. However, much work is still needed to draw a precise explanation of this phenomenon.

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11. Typical experimental procedure: Sodium formate (19 mmol), support 3 (3 g) (vide infra), 0.15 g water, and toluene (total volume 50 mL) were mixed together in a 300 mL autoclave. Reaction progress was monitored by GC. After 6–10 h at 110°C, the mixture was cooled and diluted with water and the toluene layer was evaporated to get crude biphenyl. Recrystallization of the crude product afforded 84 mol% of biphenyl<sup>14</sup> based on  $\text{C}_6\text{H}_5\text{Br}$ .
12. Procedure for the preparation of Support 3:  $\text{Na}_2\text{CO}_3$ , 2.5 g (24 mmol), TBAB, 0.2 g ( $6.2 \times 10^{-4}$  mol), 0.5 g of 5% Pd/C, and 2.525 g activated charcoal were taken in a glass reactor with 50 mL water and stirred vigorously for 3 h. The mixture was then taken to the rotavapor and dried completely under 10 mm vacuum at 70°C. The residual solid was then dried in a vacuum drier at 40°C for 70 h. The other supports were prepared in a similar manner. Support 1: Pd was supported on activated charcoal; Support 2: TBAB and Pd were both supported on carbon; Support 2A: TBAB was supported on carbon and then the solid powder mixed with Pd/C; Support 3A: similar to support 3 but the Pd/C was externally mixed with the TBAB and base supported material; Support 4: sodium formate was also supported together with the other component on Support 3.
13. A similar mechanistic approach was suggested for the Pd-catalyzed coupling of halopyridines. See: Munavalli, S.; Rossman, D. I.; Szafraniec, L. L.; Beaudry, W. T.; Rohrbaugh, D. K.; Ferguson, C. P.; Grätzel, M. *J. Fluor. Chem.* **1995**, 73, 1.
14. For a detailed description of materials and instrumentation, including the characterization of reference materials, see (a) Mukhopadhyay, S.; Rothenberg, G.; Sasson, Y. *Adv. Synth. Catal.* **2001**, 343, 274; (b) Tamura, Y.; Chun, M.-W.; Inoue, K.; Minamikawa, J. *Synthesis* **1978**, 822.