Pd/C-Catalyzed Transfer Reduction of Aryl Chlorides with Sodium Formate in Water

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Dedicated to Professor Domenico Misiti on the occasion of his 70th birthday

Keywords: Reductive dechlorination / Palladium / Catalysis / Sodium formate / Aryl chlorides

Sodium formate catalytic transfer reduction, in the presence of palladium on carbon, accomplishes not only the rapid dehalogenation of aromatic chlorocarbons in water at room temperature, but also the reduction of the aromatic moieties to alicyclic rings at 100 °C.

Introduction

The removal of halogens from aryl halides is an extremely important chemical transformation both from a preparative[1,2] and an environmental point of view.[3,4] Aromatic chlorides are much less reactive than aromatic bromides and iodides and hence, many efforts have been fueled towards the goal of efficient and clean hydrodechlorination methodologies.[5,6] Reductive cleavage is advantageous for converting halogenated organic compounds, since oxidation can generate highly toxic products such as phosgene, dioxins and chlorine, which may also poison most catalysts or, at least, lead to their deactivation. General procedures for the palladium on carbon (Pd/C) catalyzed hydrogenation of aromatic chlorides that operate under mild conditions have been applied to the hydrodechlorination of a variety of aromatic chlorides.[7,8] Multiphase systems composed of an alkaline aqueous phase and hydrocarbon solvent, such as isooctane in the presence of a phase-transfer (PT) agent, have allowed facile and selective Pd- or Pt-catalyzed hydrodehalogenation to afford dehalogenated aromatics at 50 °C and at a pressure of 1 atm of hydrogen.[9−16] However, H_2 is a gas that, for safety reasons, is not always convenient to use, and when used losses must be avoided through a carefully assembled gas delivery system. The use of a hydrogen donor has some advantages over the use of molecular hydrogen since it avoids the risks and constraints associated with hydrogen gas as well as the necessity of pressure vessels and of other equipment. Therefore, the aid of a stable hydrogen donor represents a useful alternative method to the catalytic hydrodechlorination of aromatic chlorides by molecular hydrogen. These dechlorination systems involve the use of metal hydrides,[17] metal alkoxides,[6,18] hydrosilanes,[19,20] Grignard reagents,[21] alcohols,[22] and formic acid and its salts[23,24] as the hydrogen source. Formic acid and its salts are particularly versatile, and cheap reagents that have been used as a source of hydrogen in catalytic transfer hydrogenations and have frequently been applied in the reduction of a large variety of functional groups.[25] Nevertheless, only few reports are concerned with the catalytic transfer reduction of aromatic chlorides in water.[26]

Results and Discussion

Herein, we describe a general alternative procedure for the palladium on carbon (Pd/C) catalyzed hydrodechlorination of aromatic chlorides in water, which operates under mild conditions in the presence of sodium formate as the hydrogen source. Among the noble metal catalysts tested for the hydro treatment with H_2 in the water phase of several chloro organic compounds, Pd/C showed a higher activity with respect to other noble metals.[27] In addition, Pd/C was found to be a reusable catalyst in aqueous media.[28] Initially, we investigated the Pd/C-catalyzed hydrodehalogenation reaction of 4-chlorobenzophenone (**1a**) in water in the presence of different formic acid derivatives (Scheme 1).

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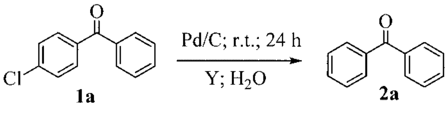
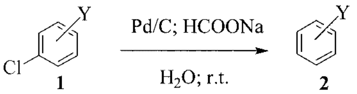


Y =	% yield
HCOOH	12
$HCOO^-NH_4^+$	33
$HCOO^-K^+$	49
$HCOO^-Na^+$	63

Scheme 1

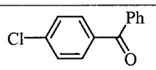
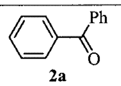
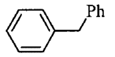
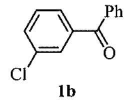
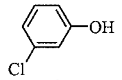
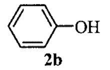
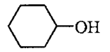
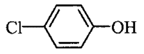
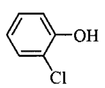
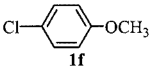
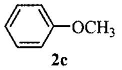
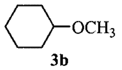
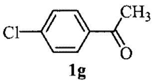
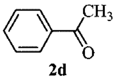
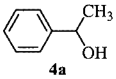
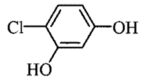
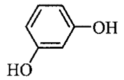
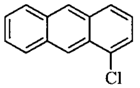
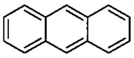
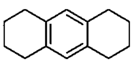
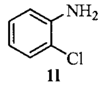
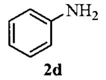
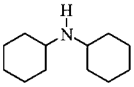
The results obtained show that HCOONa is clearly superior to the other two salts tested and to formic acid. The remaining percentage is usually accounted for by unchanged starting material. Evidence reported in the literature[29–31] show that differences in the nature of formic acid derivatives and in the reaction medium can significantly affect the reaction course. Under the optimized conditions determined above, dechlorination reactions of a variety of aryl chlorides **1** to the corresponding aromatic hydrocarbon **2** were carried out (Scheme 2; Table 1, Entries 1, 3, 4, 6, 8, 10, 12, 14, and 18).



Scheme 2

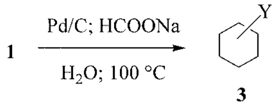
Electron-withdrawing and -donating groups in the aryl chlorides tested were well tolerated for the present catalytic dechlorination to give the corresponding aromatic products. The experimental procedure is very simple. After completion of the reaction, the catalyst was removed by filtration, and the product was isolated by extraction into a suitable organic solvent as ethyl acetate or diethyl ether. It is worth noting that the recovered Pd/C shows sufficient catalytic activity for the hydrodechlorination reaction. The activity of the recovered Pd/C was monitored by the hydrodechlorination of 2-chloroaniline (**1l**). Although the catalytic activity was gradually diminished, the yield was still 62% after it was reused for the third time. The additional parallel path to produce biphenyls by reductive dimerization[32] was not observed. By contrast with the previously reported results under our conditions, the reaction is not sensitive to the amount of water present. The Pd/C-catalyzed transfer hydrogenolysis of aryl halides by formate salts in a triphase system required the absorption of all three substrates, the aryl halide acceptor, the formate anion, and water, to a single site on the catalyst surface in a specific order.[33] No reaction was observed at all in the absence of water. It was also demonstrated that the amount of the water present in the system should be optimized to produce high reaction rates in solid/solid/liquid/liquid triphase systems.[34] Interestingly, 1-chloroanthracene (Table 1, Entry 16) leads to a mixture of anthracene (**2c**) (16%), 1,2,3,4-tetrahydroanthracene (9%), and 9,10-dihy-

Table 1. Reduction of aryl chlorides in water with HCOONa and catalytic 10% Pd/C

Entry	Substrate	Time [h]	Temperature [°C]	Product	Yield [%]
1	 **1a**	24	r.t.	 **2a**	63[a][b]
2	**1a**	24	100	 **5a**	60[a][c]
3	 **1b**	24	r.t.	**2a**	72[a][b]
4	 **1c**	3	r.t.	 **2b**	96[b][d]
5	**1c**	22	100	 **3a**	97[c][d]
6	 **1d**	3	r.t.	**2b**	100[b][d]
7	**1d**	3	100	**3a**	85[c][d]
8	 **1e**	5	r.t.	**2b**	92[b][d]
9	**1e**	16	100	**3a**	100[b][d]
10	 **1f**	13	r.t.	 **2c**	95[b][d]
11	**1f**	24	100	 **3b**	75[c][d]
12	 **1g**	24	r.t.	 **2d**	100[b][d]
13	**1g**	72	100	 **4a**	70[a][c]
14	 **1h**	2.5	r.t.	 **2e**	95[b][d]
15	**1h**	15	100	**3a**	97[c][d]
16	 **1i**	24	r.t.	 **2c**	16[b][d]
17	**1i**	24	100	 **6a**	77[a][c]
18	 **1l**	12	r.t.	 **2d**	89[b][d]
19	**1l**	12	100	 **7a**	67[c][d]

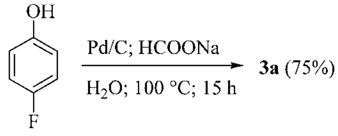
[a] Isolated yield by flash chromatography. [b] Unless otherwise stated, reactions were carried out in water with the molar ratio **1**/HCOONa/10% Pd/C = 1:5:0.05. [c] Unless otherwise stated, reactions were carried out in water with the molar ratio **1**/HCOONa/10% Pd/C = 1:15:0.05. [d] GC yield.

droanthracene (11%). This result shows us that further reduction steps could also occur. Dehalogenation and the complete reduction of aromatic chlorocarbons to alicyclic compounds is the key goal because benzene and its derivatives, as well as polycyclic aromatic hydrocarbons (PAH), are by themselves hazardous carcinogenic substances. The development of the detoxification processes that also destroy the aromatic moieties represent a target of current interest.[35] Herein, we report that the palladium-catalyzed reduction of aryl chlorides to the corresponding alicyclic compounds can be accomplished in the presence of excess HCOONa in water at reflux (Scheme 3). To the best of our knowledge, this is the first example of sodium formate catalytic-transfer reduction of aromatic chlorocarbons to their corresponding alicyclic derivatives. Hydrogenation of chlorinated aromatic derivatives to alicyclic compounds usually requires high hydrogen pressures.



Scheme 3

The best conditions so far developed (1 equiv. of aryl chloride, 15 equiv. of HCOONa in the presence of 0.05 equiv. of 10% Pd/C in H_2O at 100 °C) were usually employed when we extended the procedure to a variety of aryl chlorides as shown in Table 1. It is remarkable that under these conditions the transfer reduction of chlorophenols **1c−e** and 4-chlororesorcinol (**1h**) leads chemoselectively to the formation of cyclohexanol. By contrast with the results previously reported[36] in the hydrogenation experiments of chloroarenes in the presence of the sol-gel entrapped Pd/$[Rh(cod)Cl]_2$ or supported palladium[36] catalysts, the formation of cyclohexane and cyclohexanone, which can be regarded as the keto tautomer of the cyclohexenol, is not observed with the present methodology. Surprisingly, 4-chloroacetophenone (**1g**) can be selectively reduced to 1-phenylethanol (**4a**). Under classical conditions using methanol or ethanol as solvents and 10% Pd/C as the catalyst, the reactions proceed without any selectivity, and aromatic hydrocarbons are the sole final products.[37] The polycyclic 1-choroanthracene does not undergo exhaustive hydrogenation, but rather proceeded in a manner similar to that of previous results obtained in the reduction of anthracene;[38] 1,2,3,4,5,6,7,8-octahydroanthracene (**6a**) was isolated in good yield. The exposure of 2-chloroaniline (**1l**) to the standard conditions in Table 1 (Entry 19) leads to dicyclohexylamine (**7a**). The formation of **7a** can be viewed as occurring through the reduction of *N*-cyclohexylaniline derived by the palladium-catalyzed reductive amination of cyclohexanone imine with aniline intermediates.[39] The formation of the *N*-cyclohexylaniline was assessed by GC-MS. Finally, although this study is concerned with the hydrodehalogenation of chloroarenes, it is worth noting that fluoroarenes can easily undergo hydrodefluorination reaction. Under the conditions in Table 1, the 4-fluorophenol is converted into cyclohexanol (**3a**) in 75% yield (Scheme 4).



Scheme 4

Conclusion

In summary, we have shown that employment of Pd/C/HCOONa in water at room temperature may operate as a very mild and efficient system to accomplish the chemoselective hydrodechlorination of chloroaromatic compounds. This general catalytic process may also serve as a facile way to chemoselectively transform functionalized chloroarenes into the corresponding alicyclic derivatives in water at 100 °C. In addition to the synthetic usefulness of the reaction, demands for the treatment of industrial and natural contaminated waters is strongly motivating for the extension of this method to practical use, toward the degradation of structurally related chlorinated aromatic environmental pollutants that form unfavored benzene derivatives through conventional hydrodechlorination methods. The decontamination of water polluted by chlororganic compounds resulting from land storage of toxic wastes, industrial spills, and use of agricultural products is still an environmental emergency.

Experimental Section

General Remarks: All starting materials were commercially available and were used as purchased without further purification, unless otherwise stated. Solutions were prepared in redistilled deionized water. The products, after conventional workup, were purified by flash chromatography on silica gel, eluting with *n*-hexane/ethyl acetate mixtures. The products are all known and were identified by comparison of physical and spectroscopic data with those given in the literature.

Typical Experimental Procedure. Pd/C-Catalyzed Procedure for Hydrodechlorination of Aryl Chlorides with HCOONa at Room Temperature in Water: The aryl chlorides (1 mmol) and 10% Pd/C (0.05 mmol) were added to an aqueous solution of HCOONa (5 mmol, 4 mL). Reaction aliquots after filtration through a plug of cotton wad were analyzed by GC-MS. After completion of the reaction, the catalyst was removed by filtration, and the product was isolated by extraction into a suitable organic solvent such as ethyl acetate or diethyl ether and purified by flash chromatography of the crude mixture (silica gel; *n*-hexane/ethyl acetate mixtures).

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