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Mild and general procedure for Pd/C-catalyzed hydrodechlorination of aromatic chlorides

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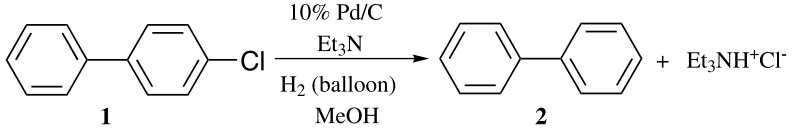
Abstract—A mild and efficient one-pot hydrodechlorination using a Pd/C–Et_3N system proceeds at room temperature, which is general for the dechlorination of a variety of aromatic chlorides.

Dehalogenation reactions of aromatic halides have important synthetic and environmental potential and can be achieved by a variety of chemical methods.[1] It is well known that aromatic chlorides are much less reactive than aromatic bromides and iodides and hence, the dechlorination of aromatic chlorides cannot readily be achieved.[1–3] Therefore, the development of new dechlorination methods remains a topic of great interest. The dechlorination of aromatic chlorides is an underdeveloped methodology, and few effective general methods are available.[2,4] Existing techniques usually utilize hydride reduction,[5] hydrogenation,[6] dechlorination using metals,[7] photolysis,[8] oxidation,[9] or electrolysis.[10] Many such reactions require high heat, high pressure, radiation, stoichiometric reagents, vast amounts of catalyst, special equipment and/or strongly basic conditions, and most of the reactions are very frequently incomplete. Herein, we describe a general procedure for the palladium on carbon (Pd/C)-catalyzed hydrodechlorination of aromatic chlorides that operate under mild conditions at room temperature and is applicable to the dechlorination of a variety of aromatic chlorides.

Recently, we have reported that addition of a nitrogen-containing base (e.g. NH_3, pyridine, ammonium acetate) to a Pd/C-catalyzed hydrogenation system as a weak catalyst poison chemoselectively inhibited the hydrogenolysis of a benzyl ether with smooth hydrogenation of other reducible functionalities such as olefin, Cbz, benzyl ester, azide and so on.[11] During the course of our further study on the chemoselective hydrogenation using the Pd/C–Et_3N system, we found that the catalytic activity of Pd/C toward the hydrodechlorination of only aromatic chlorides was remarkably and selectively **activated** by the addition of Et_3N, contrary to our expectation. Although it is suggested that dechlorination of aromatic chlorides cannot readily be achieved,[1–3] both the conversion yield and the reaction rate of the dechlorination of 4-chlorobiphenyl (**1** in Scheme 1 and Fig. 1) could be brought to outstanding levels by running the hydrodechlorination using commercial 10% Pd/C (3% of the weight of **1**) and 1.2 equiv. of Et_3N in MeOH at room temperature and under hydrogen pressure. The reaction was completed smoothly within 1 h to afford the corresponding biphenyl **2** in 100% conversion yield (GC/mass) and no products other than **2** were detected by GC/mass although the dechlorination was incomplete even after 3 days when the reaction was carried out without Et_3N (Fig. 1).

Dechlorination of 4-chlorobiphenyl (**1**) was carried out using various nitrogen-containing bases and solvents (Table 1). Typically, the reaction was carried out under ordinary hydrogen pressure (balloon) using 1.2 equiv.



1 **2**

Scheme 1. Hydrodechlorination of **1** in the presence of Et_3N.

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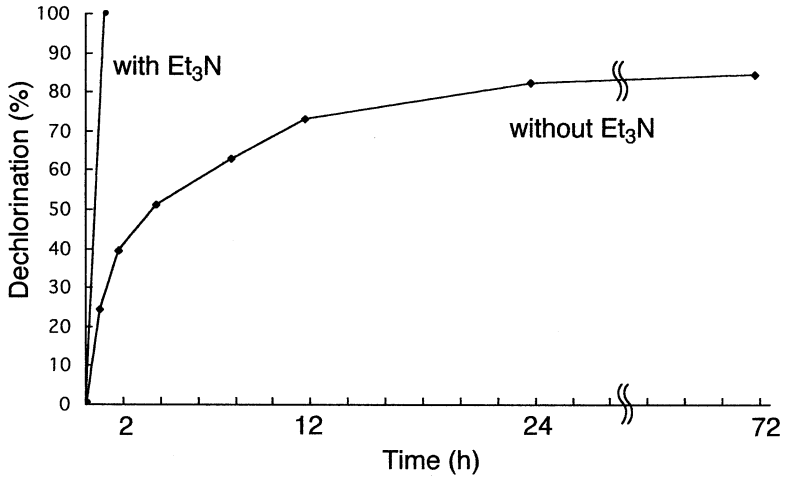


Figure 1. Kinetics plots on the hydrodechlorination of 4-chlorobiphenyl **1** using 10% Pd/C (3% of the weight of 4-chlorobiphenyl **1**) with or without Et_3N (1.2 equiv.) in MeOH under a hydrogen atmosphere at room temperature (ca. 20°C).

Table 1. Assessment of nitrogen-containing bases and solvents in the dechlorination of 4-chlorobiphenyl (**1**)[a]

Entry	Base	Solvent	Yield of **2** (%)[b]
1	None	MeOH	24
2	NH_3	MeOH	67
3	$NH_2(CH_2)_2NH_2$	MeOH	94
4	Me_2NH	MeOH	100[c]
5	Et_3N	MeOH	100[c]
6[d]	Et_3N	MeOH	100[c]
7[e]	Et_3N	MeOH	4
8	Et_3N	THF	43
9	Et_3N	Hexane	63
10	Et_3N	DMF	3
11	Et_3N	H_2O	0
12	DBU	MeOH	100[c]
13	$PhNH_2$	MeOH	100[c]
14	Pyridine	MeOH	0
15	Quinoline	MeOH	0

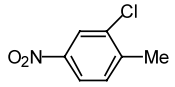
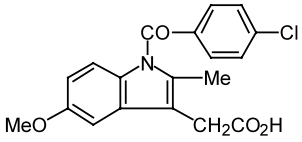
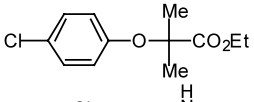
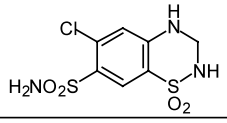
[a] All reactions were carried out under ordinary hydrogen pressure (balloon) using 1.2 equiv. of a nitrogen-containing base and 10% Pd/C (3% of the weight of the aromatic chloride) in a solvent at room temperature.
[b] Yields were determined by GC/MS.
[c] No other products were detected by GC/MS.
[d] Under dark conditions.
[e] The reaction was carried out at −20°C.

of a nitrogen-containing base and 10% Pd/C (3% of the weight of the aromatic chloride) in a solvent at room temperature and the products were detected by GC/MS and NMR after simple extraction. The use of MeOH as a solvent was found to dramatically improve the reactivity of the hydrodechlorination reaction (entries 5 and 8–11). The results shown in entries 4, 5, 12 and 13 demonstrate that the dechlorination can be carried out using relatively lipophilic amines. The dechlorination using Et_3N took place even under dark conditions (entry 6). The efficiency of the catalytic system was drastically decreased at low temperature (−20°C, entry 7). In addition, aniline, an aromatic amine, was also efficiently processed (entry 13), although, when an aromatized heterocyclic base such as pyridine or quinoline was used as a base, the hydrodechlorination was absolutely suppressed and no reaction was observed (entries 14 an 15). These facts rule out the possibility that Et_3N, an effective base, acts only as a scavenger of the generated hydrogen chloride. Thorough optimization of the reaction conditions eventually revealed that initial treatment of the methanol solution of **1** with 10% Pd/C (3% of the weight of **1**) and Et_3N (1.2 equiv.) at room temperature for 1 h under ordinary hydrogen pressure (balloon) proved to be the best reaction conditions.

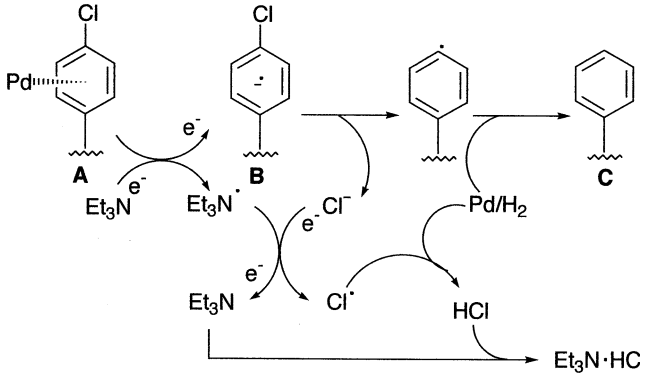
To explore the scope of this method, the hydrodechlorination of a variety of aromatic chlorides was investigated (Table 2). The results shown entries 1, 2 and 4 demonstrated that the reaction could be carried out in the presence of carboxylic acid and phenolic functionalities. Competitive reduction of the nitro moiety of 2-chloro-4-nitrotoluene was observed and the product was isolated as 4-toluidine in 90% isolated yield (entry 6), while the aromatic ketone moiety of 4-chlorobenzophenone remained somehow intact and the corresponding benzophenone was quantitatively generated (entry 3). In addition, some medicines such as indometacin (entry 7), clofibrate (entry 8) and hydrochlorothiazide (entry 9) were efficiently processed, although a prolonged reaction time was required.

There is little doubt that Et_3N is not only a scavenger of hydrogen chloride but also a strong activator of the Pd/C-catalyzed hydrodechlorination process (see Table 1). Moreover, addition of a small amount of TCNE (tetracyanoethylene) or TCNQ (7,7,8,8-tetractanoquinodimethane), a single electron capture, to the hydrodechlorination reaction mixture in the presence of Et_3N thoroughly suppresses the reaction, suggesting the participation of a single electron transfer (SET) mechanism in the simple catalytic process (Scheme 2). Initial single electron transfer to the palladium-activated chlorobenzene ring of **A** from Et_3N affords anion radical **B**, which may then convert to the dechlorinated benzene ring of **C** by subsequent elimination of the chloride anion.

Table 2. 10% Pd/C–Et_3N-mediated dechlorination of aromatic chlorides[a]

Entry	ArCl	Time (h)	Yield (%)[b]
1	4-Chlorobenzoic acid	6	100 (99)
2	2-Chlorobenzoic acid	3	100 (100)
3	4-Chlorobenzophenone	1	100 (65)[c]
4	4-Chlorophenol	3	100 (92)
5	2-Chloronaphthalene	1	100 (51)[d]
6		2	100 (90)[e]
7		25	100 (44)
8		27	100 (71)
9		22	100 (85)[f]

[a]All reactions were carried out under ordinary hydrogen pressure (balloon) using 1.2 equiv (*vs.* the number of chlorine) of Et_3N and 10% Pd/C (3% of the weight of 1) in MeOH (1% solution of 1) at room temperature for 1 h. [b] Yields were determined by GC/MS and the isolated yields are indicated in parentheses. 100% yield implied that no other products were detected by GC/MS. [c]Isolated as benzophenone. [d]The low isolated yield of the product is due to the low boiling point and volatile nature. [e]Isolated as 4-toluidine. [f]Product contaminated with 10% $Et_3NH^+Cl^-$.



Scheme 2. Tentative mechanism of the hydrodechlorination of aromatic chlorides.

In summary, we have developed a mild and efficient one-pot method for the hydrodechlorination of aromatic chlorides that proceeds at room temperature and under ordinary hydrogen pressure. The reaction is general for a variety of aromatic chlorides. The simplicity and reliability of this method makes it an attractive new tool for organic and environmental chemists.

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