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# Pd-catalyzed reduction of aryl halides using dimethylformamide as the hydride source

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**Abstract**—The Pd-catalyzed homocoupling of aryl halides in a basic DMF solution is often accompanied by the dehalogenation of the substrate as side reaction. When an inorganic base such as sodium bicarbonate is used, the reducing role of the solvent has been demonstrated using DMF-$d_7$ and GC/MS analysis.
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In the course of the study of the Pd-catalyzed 5-*endo-trig* cyclization of 1-(*o*-bromophenyl)-2-methylprop-2-en-1-ol using DMF as the solvent and an inorganic base, we have observed that a set of experimental conditions afforded 1-phenyl-2-methylprop-2-en-1-ol as a by-product.[1] The near absence of this compound when other solvents were used suggested the involvement of DMF in the hydrogenolysis process. It is known that (i) the base-catalyzed decomposition of DMF leads to carbon monoxide and dimethylamine,[2] and (ii) the reduction of arylbromides with secondary acyclic amines occurs under $Pd^0$ catalysis.[3,4] This literature information agrees with the hypothesis of DMF as the hydride source of the above Pd-catalyzed hydrodehalogenation. In fact, the possible involvement of DMF in a Pd-catalyzed reduction has already been envisaged.[5,6] Heitz et al. have observed the formation of dehalogenated bromoarenes as side products in the course of their Pd-catalyzed coupling using triethylamine as base and DMF as solvent.[5] Experimental conditions using $DCONCD_3$, $N(CD_2CH_3)_3$ and $N(CH_2CD_3)_3$ have, however, indicated a dehalogenation occurring through a H-transfer from the methylene of the tertiary amine.[5] Fiaud et al. have reported that the Pd-catalyzed substitution of 3- and 4-quinolylmethyl acetates was accompanied by some hydrogenolysis of the C–OAc bond when DMF

was used as the solvent.[6] To investigate the nature of the reducing agent, these authors have carried out reactions in DMF-$d_7$, but no reduction product was then detected.[6] The above observations and comments urged us to examine the hydrodehalogenation of various aryl halides using DMF, base and catalytic amounts of palladium.[7,8]
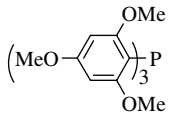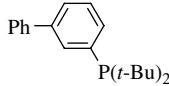
Various conditions have been tested using 2-bromonaphthalene (**1**) as the substrate (Table 1). The reaction at 120 °C in DMF with $Pd(OAc)_2$ as the catalyst and $KF/Al_2O_3$ as the base,[9] led to naphthalene (**2**) and to the corresponding binaphthyl,[10] the **2/1** ratio being 23:77 after 18 h (run 1). Switching to $PdCl_2$ as the catalyst without ligand (run 2) or with ligands such as $PPh_3$ and dppb (runs 3 and 4) led to lower **2/1** ratios. In contrast, other ligands, especially dppf, improved this ratio (runs 5–7), in particular when $NaHCO_3$ was used as the base (run 8). With this base, the $PdCl_2/PPh_3$ catalytic system led, as previously (run 3), to low amounts of **2** (run 9). In *o*-xylene instead of DMF as solvent, the $PdCl_2/dppf$-catalyzed reaction was sluggish and led only to trace amounts of **2** (run 10). The above results highlight the ligand-dependent and solvent-dependent hydrodebromination of **1**.

The above optimum catalytic system has then been tested on other aryl halides (Table 2). With 1-bromonaphthalene, an increase of the reaction temperature and time was required for a fair conversion (runs 1–4). These modifications were also necessary with bromobenzene and 4-bromobiphenyl as substrates (runs

**Table 1.** Hydrodebromation of 2-bromonaphthalene under various conditions[a]

| Run | Catalyst | Ligand[b] | Base | 1 / 2 [c] |
|---|---|---|---|---|
| 1 | Pd(OAc)$_2$ | No | KF/Al$_2$O$_3$ | 77:23 |
| 2 | PdCl$_2$ | No | KF/Al$_2$O$_3$ | 92:8 |
| 3 | PdCl$_2$ | PPh$_3$ | KF/Al$_2$O$_3$ | 89:11 |
| 4 | PdCl$_2$ | dppb | KF/Al$_2$O$_3$ | 87:13 |
| 5 | PdCl$_2$ | (MeO—⬡(OMe)(OMe)—P)$_3$ | KF/Al$_2$O$_3$ | 57:43 |
| 6 | PdCl$_2$ | Ph—⬡—P(t-Bu)$_2$ | KF/Al$_2$O$_3$ | 57:43 |
| 7 | PdCl$_2$ | dppf | KF/Al$_2$O$_3$ | 10:90 |
| 8 | PdCl$_2$ | dppf | NaHCO$_3$ | 2:98 |
| 9 | PdCl$_2$ | PPh$_3$ | NaHCO$_3$ | 94:6 |
| 10[d] | PdCl$_2$ | dppf | NaHCO$_3$ | >99:<1 |

[a] Reactions were carried out at 120 °C for 18 h using Pd-catalyst (0.05 equiv), ligand (0.1 equiv), NaHCO$_3$ (1.1 equiv) or KF/Al$_2$O$_3$ (500 mg/mmol of substrate) in anhydrous DMF (2 mL per mmol of substrate) under an argon atmosphere.
[b] dppb: 1,4-bis(diphenylphosphino)butane; dppf: 1,1′-bis(diphenylphosphino)ferrocene.
[c] The 2-bromonaphthalene/naphthalene ratio was estimated from GC analysis using an HP 6890 apparatus equipped with DB1 capillary column (length: 25 m, diameter: 0.32 mm) and an HP 3395 integrator.
[d] Reaction carried out using *o*-xylene as the solvent.

5–10). Similar experimental conditions led to full conversion of aryl iodides with the production of both reduction and diaryl compounds (runs 11–15). In contrast, only traces of benzene were detected from chlorobenzene (run 16). Aryl dibromides led to mixtures containing the corresponding arenes and aryl monobromides (Table 3).
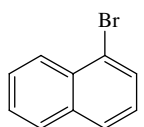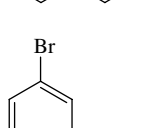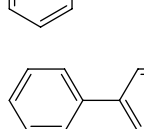
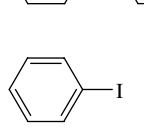**Table 2.** Hydrodehalogenation of aryl halides[a]
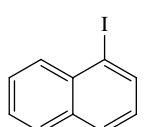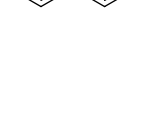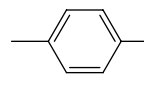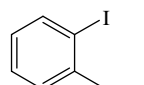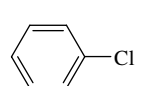
| Run | ArX | t (°C) | Time (h) | ArX/ArH[b] |
|---|---|---|---|---|
| 1 | 1-bromonaphthalene | 120 | 18 | 94:6 |
| 2 | | 150 | 18 | 79:21 |
| 3 | | 150 | 48 | 44:56 |
| 4 | | 150 | 72 | 2:98 |
| 5 | bromobenzene | 120 | 18 | 96:4 |
| 6 | | 150 | 18 | 57:43 |
| 7 | | 150 | 48 | 15:85 |
| 8 | | 150 | 72 | 0:100 |
| 9 | 4-bromobiphenyl | 120 | 18 | 92:8 |
| 10 | | 150 | 18 | 7:93 |
| 11 | iodobenzene | 120 | 18 | 92:8 |
| 12 | | 150 | 18 | 0:100 |
| 13 | 1-iodonaphthalene | 150 | 48 | 0:100 |

**Table 2** (*continued*)

| Run | ArX | t (°C) | Time (h) | ArX/ArH[b] |
|---|---|---|---|---|
| 14 | 4-iodotoluene | 150 | 48 | 0:1000 |
| 15 | 2-iodotoluene | 150 | 18 | 0:100 |
| 16 | chlorobenzene | 150 | 48 | 97:3 |

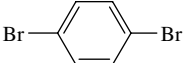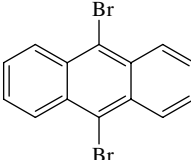[a] Reactions carried out using PdCl$_2$ (0.05 equiv), dppf (0.1 equiv), NaHCO$_3$ (1.1 equiv) in anhydrous DMF under an argon atmosphere.
[b] Ratios estimated from GC analysis.

The literature on the reactivity of DMF,[2] the Pd-catalyzed reduction of arylbromides with secondary acyclic amines,[3,4] and the absence of the reduction product when using *o*-xylene as the solvent (Table 1, run 10) suggests the mechanism depicted in Scheme 1 for the above hydrodehalogenations. Intermediate **A**, formed by the insertion of Pd$^0$ into the Ar-X bond, would react with dimethylamine to yield **B** that should suffer a β-H elimination.[12] Reductive elimination of Pd$^0$ from the resulting hydridopalladium complex (**C**) would give ArH.

To establish the validity of the above mechanism, the reaction of 2-bromonaphthalene was carried out in DMF-$d_7$ under conditions of run 8, Table 1. Two

**Table 3.** Hydrodebromation of aryl dibromides[a]

| Run | BrArBr | t (°C) | Time (h) | BrArBr/BrArH/HArH[b] |
|-----|--------|--------|----------|----------------------|
| 1[c] | Br—⟨benzene⟩—Br | 150 | 48 | 70:24:6 |
| 2[c] | ⟨9,10-dibromoanthracene⟩ | 150 | 48 | 27:68:5 |
| 3[d] | | 120 | 18 | 19:75:6 |

[a] Reactions carried out using PdCl$_2$, dppf and NaHCO$_3$ in anhydrous DMF under an argon atmosphere.
[b] Ratios estimated from GC analysis.
[c] PdCl$_2$: 0.05 equiv, dppf: 0.1 equiv, NaHCO$_3$: 1.1 equiv.
[d] PdCl$_2$: 0.1 equiv, dppf: 0.2 equiv, NaHCO$_3$: 2.2 equiv.
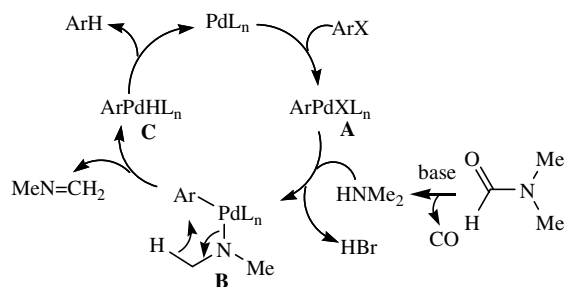


**Scheme 1.**

predictions can be made for this reaction. Firstly, the arene product should contain a single deuterium. Secondly, the 2-bromonaphthalene/naphthalene ratio should increase since the β-hydrogen elimination would be slower as a result of a primary isotope effect.[13] As expected, the bromonaphthalene/naphthalene ratio increased, 52:48 instead of 2:98, and the GC/MS analysis of the crude mixture showed the formation of monodeuterated naphthalene (compare Graphs 1 and 2). Given the mass spectra, the reduction product is not completely deuterated;[14] this could be due to scrambling with trace amounts of water.

Given the competing formation of the biaryl compounds, it is clear that the above Pd-catalyzed hydrodehalogenation of aryl halides is not a synthetically useful procedure. Nevertheless, these studies reveal a new possible role of DMF: besides being a source of carbon monoxide[2,15,16] and dimethylamine,[2,16,17] DMF is also a hydride source via a Pd-catalyzed reaction with the in situ produced dimethylamine.[18] This observation
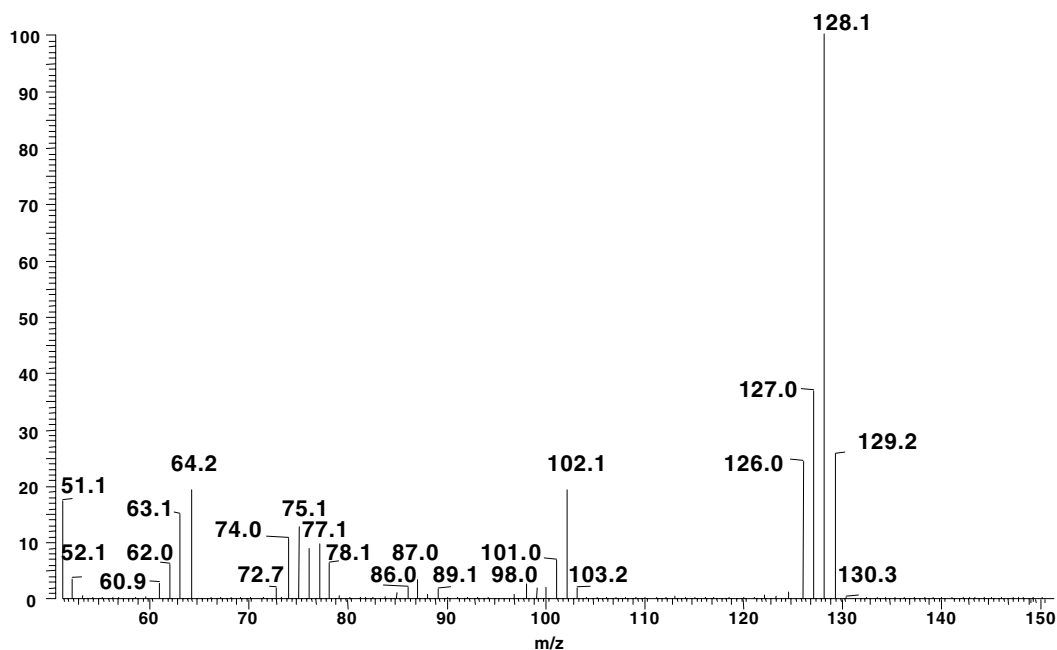


**Graph 1.** Mass spectrum of the reduced compound obtained from 2-bromonaphthalene in DMF.
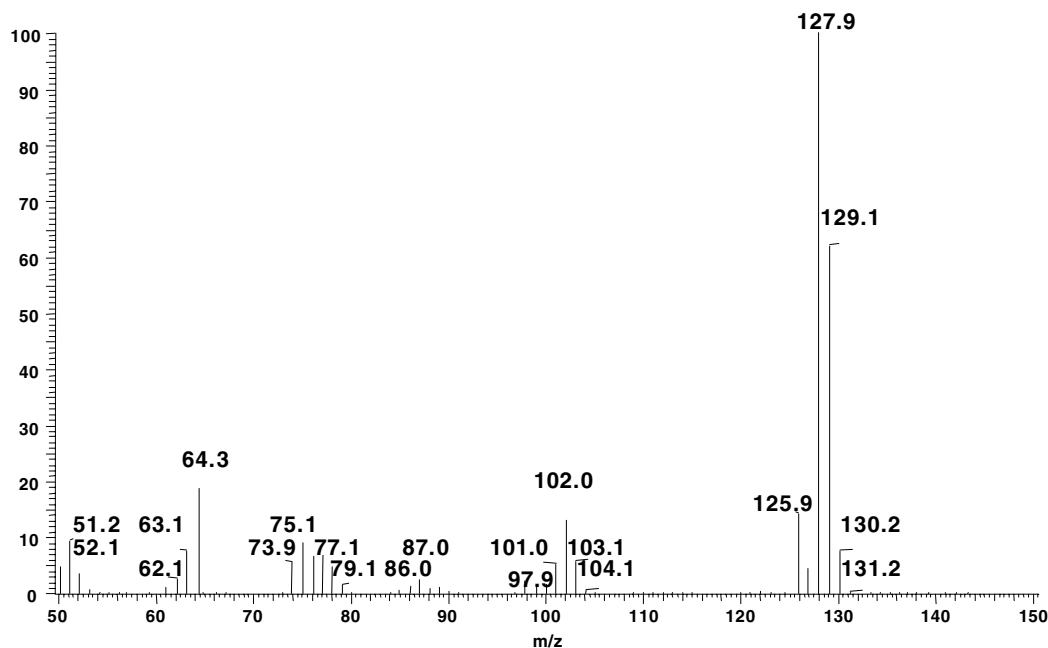
**Graph 2.** Mass spectrum of the reduced compound obtained from 2-bromonaphthalene in DMF-$d_7$.

could, in some cases, explain the increase in the performance of Pd-catalyzed reductions when they are carried out in DMF.[19]

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