Communications

Palladium Hydrides in Organic Synthesis. Reduction of Aryl Halides by Sodium Methoxide Catalyzed by Tetrakis(triphenylphosphine)palladium

Summary: Aryl halides react with sodium methoxide and catalytic amounts of tetrakis(triphenylphosphine)palladium in DMF at ~100 °C to produce arenes.

Sir: We have undertaken the investigation of new applications of transition metal hydrides as intermediates in organic synthesis.[1] Of the several methods for the generation of these hydrides, the most common are reactions of transition metal complexes with hydrogen or main group hydrides. Another common method, the reaction of various complexes with alcohols in the presence of base or with alkoxides,[2] is especially attractive because of the ready availability and low cost of these materials as sources of hydride.

For our initial studies, we chose to examine the reduction of organic halides. In synthesis, the need occasionally arises to remove a halogen atom that has been introduced to temporarily block a given position, as an activating group, or as the side result of other synthetic operations.[3] We now wish to report a new method for the reduction of aryl halides to arenes catalyzed by tetrakis(triphenylphosphine)palladium(0) (1)[4] with sodium methoxide as the source of hydride (eq 1). Typical results of this reaction are summarized in Table I.

$$\mathrm{ArX} + \mathrm{NaOCH_3} + 0.05\ \underset{\textbf{1}}{\mathrm{Pd(PPh_3)_4}} \xrightarrow[\mathrm{DMF}]{\sim 100\ ^\circ\mathrm{C}} \mathrm{ArH} \qquad (1)$$

Commercially available sodium methoxide is satisfactory for this reaction. Normally, an excess (50%) is employed in order to allow for possible decomposition during storage and handling, although if adequate precautions are taken, the use of this excess is not necessary. Both this reagent and the catalyst (1) may be weighed conveniently in the air and then transferred to the reaction vessel which is then placed under an inert atmosphere for the duration of the reaction. *N,N*-Dimethylformamide (DMF) is normally used as the solvent for this reaction, but other polar solvents may also be employed. For example, with either ethanol or methanol as the solvent, ~80% yields of benzene are obtained from bromobenzene. Also, methoxide is not the only alkoxide which may be employed in the reduction. For example, sodium isopropoxide[5] reacts with 2-bromonaphthalene in DMF at 60 °C for 6 h to give naphthalene in 62% yield (94% conversion of the bromide). Despite the higher reaction temperature required for the use of methoxide, we have chosen to emphasize the use of this reagent in our initial studies because of the convenience provided by its air stability and commercial availability.

The principal utility of the reaction is the reduction of aryl bromides. Chlorobenzene (run 13) undergoes only a very low conversion under our usual conditions. The presence of a nitro substituent (runs 9 and 10) increases the rate of the reaction, but the reduction product is accompanied by a considerable amount of coupling product, the corresponding biaryl (Ar–Ar). Coupling is also observed for a substrate bearing a carbomethoxy substituent (run 8) and for iodobenzene (run 12). For the remaining cases, the yields of biaryls are generally quite low (0–2%). Other side products are *N,N*-dimethylanilines ($\mathrm{ArNMe_2}$, 0–5%) and anisoles ($\mathrm{ArOCH_3}$, 0–1%). Also, small amounts of benzene (~10% yields based upon the amounts of aryl halides) have been detected in several cases (e.g., runs 2–4) in which this product could not be formed from the starting aryl halide.[6]

Table I. Reduction of Aryl Halides

Run	Aryl halide	Time, h	Temp, °C	Conversion, %	Yield of ArH, %[a]
1	Bromobenzene	4.5	95	100	89
2	2-Bromotoluene	5.0	95	100	89
3	4-Bromotoluene	4.5	100	100	70
4	2-Bromonaphthalene	4.0	100	100	85[b]
5	1-Bromonaphthalene	4.0	120	78	84
6	4-Bromophenyl phenyl ether	4.0	100	100	81[b]
7[c]	Sodium 3-bromobenzoate	3.5	140	58	100
8	Methyl 3-bromobenzoate	4.0	100	95	54[d]
9	4-Chloronitrobenzene	4.0	100	100	43[d]
10	4-Bromonitrobenzene	4.5	100	100	39[d]
11[c]	Sodium 4-bromophenoxide	4.0	100	[e]	36
12	Iodobenzene	4.0	80	100	44[d]
13	Chlorobenzene	3.0	100	1	50

[a] Unless otherwise noted, the yields were determined by GLC with an internal standard. All yields are based upon the amounts of aryl halides consumed. [b] This value is an isolated yield. [c] The sodium salt was formed in situ from the neutral compound by use of an additional equivalent of sodium methoxide. [d] This product was accompanied by large amounts of the corresponding biaryl (~30–50% yield). [e] The conversion was not determined in this case.

A number of other methods have been reported for the reduction of aryl halides,[7] some of the more important methods being the use of catalytic hydrogenolysis,[8] Raney nickel,[9] lithium aluminum hydride,[10] organotin hydrides,[11] and copper hydrides.[12] The advantages of our method over these earlier approaches are the use of a very simple, readily available, inexpensive, and comparatively nonhazardous source of hydride, better functional group compatibility than several of the other methods (see runs 7–10), the catalytic use of the metal species, and the simplicity and convenience of performing the reaction using routine laboratory glassware.

A likely pathway for the reaction is outlined in Scheme I. Oxidative addition[13] of the aryl halide to a coordinatively unsaturated zerovalent palladium complex is followed by metathetical displacement of halide from the adduct **2** to give the methoxo complex **3**, which then forms the hydride complex **4** and formaldehyde. Finally, reductive elimination of the arene from **4** regenerates the catalyst. The steps leading from **2** to the arene are well-precedented in earlier work,[2c,14] including the oxidation of alcohols to carbonyl compounds by palladium salts.[15] Because we have been unable to detect formaldehyde in our reaction mixtures, we doubt whether it is produced in free form, but it probably undergoes further oxidation as has been reported for other systems.[16] To date we have made no attempts to identify other products derived

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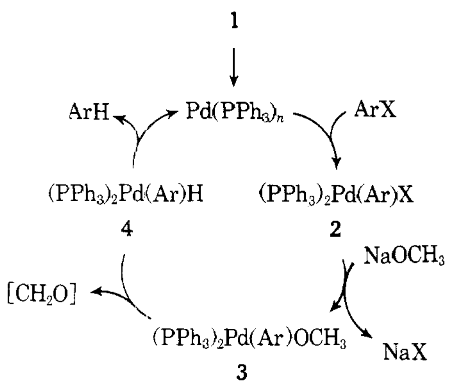
Scheme I



from the formaldehyde or possibly from the solvent, DMF. Also, the nature of the palladium species remaining after completion of the reaction has not been investigated. Therefore, we cannot rule out other possible mechanisms at this time.

The formation of the various side products is explainable on the basis of Scheme I. Biaryls have previously been obtained from arylpalladium complexes.[17] Reductive elimination from **3** would produce anisoles, and metathetical displacement of halide from **2** by the *N*,*N*-dimethylamide ion derived from DMF would lead to anilines. Formation of benzene may result from cleavage of a carbon–phosphorus bond of the triphenylphosphine ligand, a process for which several other workers have reported evidence.[18]

A typical procedure is given for the reduction of 2-bromonaphthalene (run 4). Into a round-bottom flask equipped with a magnetic stirring bar were placed 2-bromonaphthalene (0.414 g, 2.00 mmol), sodium methoxide (0.162 g, 3.00 mmol), and **1** (0.116 g, 0.100 mmol) at 25 °C. The mixture was then placed under nitrogen, DMF (4 mL) was added, and the heterogeneous yellow mixture was heated at 100 °C for 4 h. The resulting orange solution was cooled to 25 °C and diluted with ether, water, and pentane. The crude product was isolated from the organic layer and was purified by sublimation [75–140 °C (16 Torr)] to afford 0.218 g (85%) of naphthalene as white crystals, mp 79–80 °C (lit.[19] mp 80.2 °C).

Further work is in progress to explore other conditions for performing the reduction,[20] the generation of the catalyst in situ, the use of other transition metal species as catalysts, and the reduction of other types of organic halides and of other classes of compounds. We also intend to investigate conditions for obtaining the biaryls as the major products because of the important potential of this reaction to provide a metal-*catalyzed* method for the coupling of aryl halides as opposed to the usual methods which employ stoichiometric amounts of metal-containing reagents.[21–23]

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(22) An approach to optimization of biaryl formation is to employ a reducing agent which is capable of reducing Pd(II) to the catalytically active Pd(0) species but which does not lead to reduction of the aryl halides.

(23) Because the biaryls could conceivably have been formed from the arenes (the reduction products) by the well-known Pd(II)-catalyzed arene coupling reaction,[24] a control experiment was performed in which 2-bromotoluene was reduced under the usual conditions but in the presence of 1 equiv of benzene. No (<0.1%) biphenyl or methylbiphenyls were formed. Therefore, the biaryl side products are probably formed by a direct coupling of the aryl halides.

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1,2-Transposition of Ketones via Vinylsilanes

Summary: New methodology for shifting a ketone carbonyl by one carbon is described. The scheme, which involves sequential vinylsilane generation from an arenesulfonyl hydrazone, epoxidation, hydride reduction, and chromic acid oxidation, is both simple and efficient.

Sir: The carbonyl group plays a pivotal role in bringing latitude to organic synthesis. The need to relocate this functional group within a molecule occurs with such frequency that interest in efficient methods of carbonyl transposition remains high. Various procedures have been developed for effecting site exchange within saturated[1–9] and α,β-unsaturated ketones,[10–13] sometimes in tandem with an alkylation step,[14–17]

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