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Communication

Synthesis of alkyl- and aryldiphenylphosphines via electrogenerated magnesium chloride diphenylphosphanide

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Abstract

A two-steps procedure allowing the formation of alkyldiphenylphosphines and aryldiphenylphosphines in good yield is described. It relies on the electrochemical preparation of magnesium chloride diphenylphosphanide and its subsequent coupling with either alkyl halides or aryl fluorides.

Keywords: Alkyldiphenylphosphine; Aryldiphenylphosphine; Chlorodiphenylphosphine; Organic halide; Electrosynthesis; Diphenylphosphanide

Phosphines are of high interest in homogeneous catalysis due to their broad activity as ligands. Since the pioneering work of Stille [1] concerning the palladium-catalyzed formation of triarylphosphines, several studies have been devoted to transition metal-catalyzed cross-coupling reactions leading to arylated phosphines. For example, aryl triflates react with diphenylphosphine in the presence of palladium- [2] or nickel-based catalysts [3]. Aryldiphenylphosphine can be obtained through palladium-catalyzed couplings of triphenylphosphine with either aryltriflates [4] or aromatic bromides [5]. Some years ago, it was reported that nickel complexes $NiCl_2(dppe)$ [6] or $NiCl_2(PPh_3)_2$ [7] are efficient catalysts for the synthesis of triarylphosphines through reductive coupling of aryl triflates with chlorodiphenylphosphine. In related approaches, it was shown in this laboratory that a the $NiBr_2(bpy)$ catalyzed cross-coupling can be achieved by an electrochemical way [8] or using a zinc-mediated reductive coupling between aryl halides and chlorodiphenylphosphine in heated NMP (*N*-methylpyrrolidin-2-one) [9].

Another synthetic pathway based on the formation of carbon nucleophiles and the subsequent coupling with chlorophosphines has also been widely employed [10]. Thus, starting from aryl halides, lithium–halogen exchange [11,12] or Grignard reagents synthesis [12a] allows the formation of strong nucleophiles which easily displace chlorodiphenylphosphine giving rise to the formation of aryldiphenylphosphines in generally good yield. In a paper, Knochel et al. have reported that aliphatic or some aromatic organozinc compounds can also be coupled with chlorophosphines [13].

Two-steps procedures relying on the use of potassium diphenylphosphanide were also employed [14,15]. Thus, it was shown that this nucleophile reacts efficiently with *ortho*-substituted aryl fluorides to yield aryldiphenylphosphines in high yield [15].

Among the numerous topics developed in this laboratory, the electrochemical activation of halogenated species is of constant interest. Indeed, reactions proceed generally smoothly and do not require the use of drastic conditions. Thus, several years ago, it was shown by Folest et al. that chlorodiphenylphosphine can be electrochemically coupled with some alkyl halides in a one-step reaction leading to alkyldiphenylphosphines [16]. As a part of our program

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devoted to the electrochemical activation of heteroaromatic compounds we decided to reinvestigate this procedure and envisaged a stepwise approach towards such compounds. Thus, we now report herein a convenient synthesis of various alkyl- and aryldiphenylphosphines starting from chlorodiphenylphosphine and organic halides, and involving the electrochemical preparation of magnesium chloride diphenylphosphanide as the key step.

In the laboratory, it was previously shown that one-step coupling reactions occur upon electroreduction of a mixture of chlorodiphenylphosphine and alkyl halides using a consumable magnesium anode [16]. The scope of the reaction was somewhat limited by the obligation to use aliphatic haloalcanes to avoid electrochemical side-reactions. This behaviour was confirmed within the framework of a preliminary study in which mixtures of benzyl halide and chlorodiphenylphosphine were exposed to electroreduction using a sacrificial magnesium anode. Indeed, only a small amount of the wanted benzyldiphenylphosphine was detected in reaction mixtures while toluene and bibenzyl were formed in large amounts. Then, in order to extend the scope of the reaction, we decided to set up a stepwise protocol in which the first step would be the electroreduction of chlorodiphenylphosphine. Thus, our first goal was to find the most simple and efficient conditions to achieve the electrochemical activation of chlorodiphenylphosphine as its Grignard-related form, magnesium chloride diphenylphosphanide. Independently, it was previously shown in the laboratory that the use of a sacrificial magnesium electrode process in dimethylformamide can allow the conversion of aromatic amines into convenient nucleophiles for the displacement of aliphatic halides [17]. Thus, it was postulated that related reaction conditions could be adapted to the activation of chlorodiphenylphosphine and indeed the hypothesis was confirmed on the base of preliminary electrochemical reductions which revealed the formation of nucleophilic species in the reaction medium upon reaction with benzyl iodide. Using this test-reagent, it was found that no phosphanide was present in the reaction medium until a charge corresponding to ca. 1 F/mol charge was passed while a charge corresponding to ca. 2.5 F/mol (e.g. 2500 C for 10 mmol of Ph_2PCl) was the optimum value for the completion of the electrolyses.

During the course of the electrolyses, which were carried out at a constant current intensity of 0.2 A, the cathodic potential was monitored. It was remarked an evolution from ca. −1.4 V vs. SCE to ca. −2 V versus SCE after a charge corresponding to ca. 1 F/mol was passed. This observation is consistent with the electroreduction of Ph_2PCl into Ph_2PMgCl (at ca. −1.4 V versus SCE) which fast react with remaining Ph_2PCl to provide the dimeric compound $Ph_2P–PPh_2$ which is further reduced at a lower reduction potential (ca. −2 V versus SCE). This formal ECE mechanism is depicted in Scheme 1.

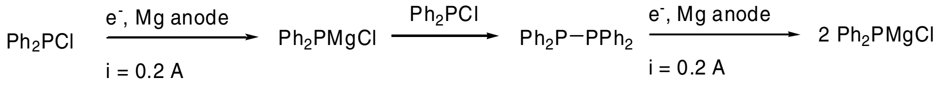
The difficulty to reduce $Ph_2P–PPh_2$ into the corresponding phosphanide Ph_2P^-, as attested by such a reduction potential, could be confirmed in a chemical experiment involving chlorodiphenylphosphine and magnesium powder. Indeed, the very exothermic reaction gave rise to the exclusive formation of $Ph_2P–PPh_2$ which proved to be very sensitive to moisture but could be nevertheless detected using GC/MS. Such reduction potentials are also consistent with previous results which revealed that one-step electroreductive couplings of chlorodiphenylphosphine and benzyl halides are inefficient. This behavior can be attributed to the competitive reduction of $Ph_2P–PPh_2$ and these halides which can occur near −2 V (versus SCE). Such results might also be predicable with aryl iodide and some carbonyl- or nitrile-bearing benzenes which are also reducible compounds. Thus, the use of a two-step procedure was essential to circumvent such drawbacks. Following typical experimental conditions [18], alkyl halides and aryl fluorides were then exposed to the electrogenerated phosphanide and allowed to react for few hours at room temperature.

Results are presented in Table 1.

Yields of alkyl- and aryldiphenylphosphines [20] are generally good, ranging from 35% to 85%. It can be noted that yields can be improved by using a slight overstoechiometric amount of chlorodiphenylphosphine at the electrolysis step. This behaviour can be clearly illustrated with comparison of entries 3 and 4 of Table 1 or 9 and 14 of Table 1 for which yields were improved from 38% to 83% or from 50% to 84%, respectively. The residual water which can be present in the solvent might be responsible of the consumption of a part of chlorodiphenylphosphine thus requiring the use of a slight excess of this starting compound.

It is noteworthy that *ortho*-but also *meta*-substituted aryl fluorides react efficiently, best results being nevertheless obtained with electron-withdrawing substituents located at the *ortho* position. These results are consistent with a SNAr-type reaction mechanism in which aryl fluorides are also known to react more efficiently than aryl chlorides. This could be obviously confirmed by an experiment (entry 11 of Table 1) which showed that in the presence of both fluoride and chloride connected to the phenyl moiety, only the fluoride is displaced by the phosphanide.

On the other hand, we decided to test the scope of the reaction and some preliminary experiments involving chlorodiphenylphosphine and aryl bromides were conducted in this goal. It could be observed that such couplings do not proceed in standard conditions described below [18] but require heating in the presence of a metal-transition cata-

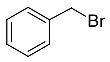
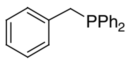
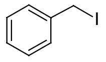
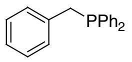
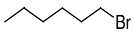
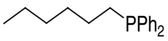
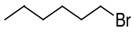
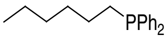
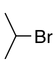
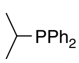
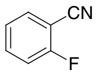
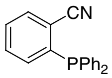
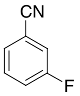
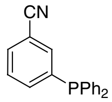
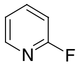
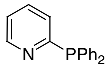
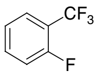
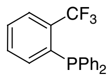
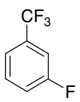
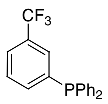
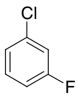
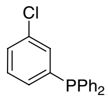
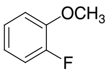
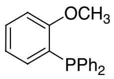
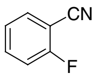
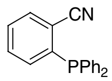


$$Ph_2PCl \xrightarrow[i\,=\,0.2\,A]{e^-,\ Mg\ anode} Ph_2PMgCl \xrightarrow{Ph_2PCl} Ph_2P{-}PPh_2 \xrightarrow[i\,=\,0.2\,A]{e^-,\ Mg\ anode} 2\ Ph_2PMgCl$$

Scheme 1.

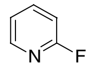
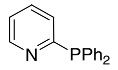
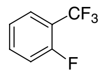
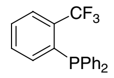
Table 1
Coupling of magnesium chloride diphenylphosphanide with organic halides

$$Ph_2P{-}Cl \xrightarrow[\text{DMF}]{e^-,\ \text{Mg anode}} Ph_2PMgCl \xrightarrow{RX} Ph_2P{-}R$$

Entry	RX	Coupling time (min)	Product		Isolated yield (%)
1		120		**1**	60[a]
2		60		**1**	68[a]
3		45		**2**	38[a]
4		30		**2**	83[b]
5		45		**3**	68[b]
6		30		**4**	70[a]
7		45		**5**	47[a]
8		15		**6**	67[a]
9		30		**7**	50[a]
10		45		**8**	35[a]
11		120		**9**	52[a]
12		120		**10**	Traces[a]
13		30		**4**	85[b]

(continued on next page)

Table 1 (*continued*)

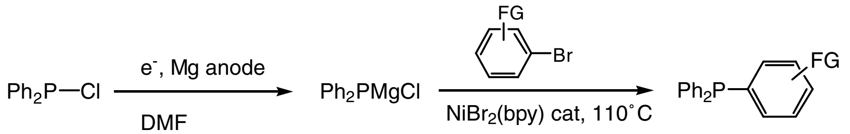
Entry	RX	Coupling time (min)	Product		Isolated yield (%)
14		30		**6**	76[b]
15		30		**7**	84[b]

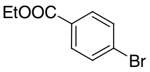
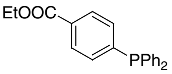
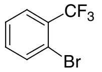
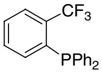
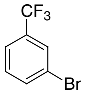
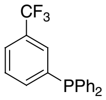
[a] 10 mmol Ph_2PCl and RX were used.

[b] Based on starting halide, 15 mmol Ph_2PCl and 10 mmol RX were used.

Table 2

Catalyzed coupling of magnesium chloride diphenylphosphanide with aryl bromides



Entry	ArBr	Coupling time (min)	Product		Isolated yield (%)
1		24		**11**	26[a]
2		15		**7**	63[a]
3		24		**8**	52[a]

[a] 10 mmol Ph_2PCl and ArBr were used.

lyst which, under the form of $NiBr_2$ associated with bipyridine, was found to be rather efficient.

These preliminary results are reported in Table 2.

In conclusion, the results reported in this paper show that the electrochemical activation of chlorodiphenylphosphine as its magnesium chloride diphenylphosphanide form and its subsequent coupling with alkyl halides or aryl fluorides can be realized in an efficient manner. The major advantage of this method relies on the use of mild and simple reaction conditions since electrolyses and couplings are conducted at room temperature. Electrolytic magnesium chloride diphenylphosphanide can also be coupled with an aryl bromide provided that a nickel complex is added in a catalytic amount.

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[18] In a typical procedure, the electrochemical cell [19] fitted with a magnesium rod as the anode and a stainless steel grid as the cathode was flushed with argon. Dimethylformamide (30 mL) was added using a syringe. To the solution was added tetrabutylammonium tetrafluoroborate (0.5 g) as supporting electrolyte and dichlorophenylphosphine (10 mmol). A constant current intensity of 0.2 A was applied until a charge of 2500 C was passed. The organic halide (10 mmol) was added and after few hours at room temperature, the reaction was quenched using a 5% hydrochloric acid solution. The resulting mixture was extracted with dichloromethane and the organic layer evaporated to dryness. Crystallization of the resulting crude oil in ethanol or chromatographic purification over silica gel using a pentane/ether mixture as an eluent afforded the analytically-pure phosphine derivative.

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[20] Coupling products were characterized using ^{1}H NMR (200 MHz, $CDCl_3$), ^{13}C NMR (50 MHz, $CDCl_3$) when required, ^{19}F NMR (188 MHz, $CDCl_3$), ^{31}P NMR (80 MHz, $CDCl_3$) and mass spectroscopy. Data for selected compounds: *n-Hexyldiphenylphosphine (**2**)*: ^{1}H NMR, δ (ppm): 0.65–0.85 (m, 3H), 1.10–1.40 (m, 8H), 1.90–2.05 (m, 2H), 7.18–7.36 (m, 10H); ^{31}P NMR, δ (ppm): -21.14; MS, *m/z* (relative intensity): 270 (M, 38), 241 (M-29, 12), 213 (M-57, 24), 200 (M-70, 44), 199 (M-71, 100), 186 (M-84, 50), 183 (M-87, 45), 108 (M-162, 26). *(3-Diphenylphosphino)benzonitrile (**5**)*: ^{1}H NMR, δ (ppm): 7.80–7.20 (m, 14H); ^{31}P NMR, δ (ppm): -10.04; MS, *m/z* (relative intensity): 287 (M, 100), 208 (M-79, 33), 183 (M-104, 36), 108 (M-179, 35). *Diphenyl(3-(trifluoromethyl)phenyl)phosphine (**8**)*: ^{1}H NMR, δ (ppm): 7.80–7.10 (m, 14H); ^{31}P NMR, δ (ppm): -9.99; ^{19}F NMR, δ (ppm): -62.38; MS, *m/z* (relative intensity): 330 (M,100), 251 (M-79,19), 203 (M-127, 18), 183 (M-147, 48), 108 (M-222, 22).