ORGANIC LETTERS

2009
Vol. 11, No. 8
1689−1692

Preparation of Diphenyl Phosphide and Substituted Phosphines using Alkali Metal in Silica Gel (M−SG)

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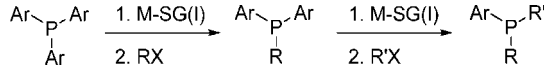
Received February 2, 2009

ABSTRACT



Alkali metals absorbed in silica gel (the M−SG reagents) efficiently cleave C−P bonds in triaryl- and diarylphosphines. The resulting alkali metal phosphides can serve as useful building blocks for a variety of phosphines. Alkyldiarylphosphines undergo exclusive aryl group cleavage.

Diaryl phosphides of alkali metals are important organic reagents for many organic transformations such as dehydroxylation of α-hydroxy ketones,[1] stereoselective reduction of *gem*-dihalides,[2] regio- and stereospecific cleavage of silylated and stannylated epoxides,[3−5] demethylation of methylammonium salts[6] and methyl aryl ethers,[7] stereoselective displacements of secondary mesylates and tosylates in steroids,[8] the Staudinger-type reaction[9] and bromouracil functionalization.[10] Diaryl phosphides are also key building blocks for the many substituted phosphine[11−16] ligands that enable homogeneous catalytic processes including hydroformylations,[17] asymmetric hydrogenations, and other asymmetric syntheses.[18,19]

Literature routes to alkali metal phosphides generally use the reaction of the alkali metal with diaryl-,[20,21] diarylhalo-,[22] or triarylphosphines.[23] This last reaction[24−27] has the advantage that many triarylphosphines are commercially available and air stable.[28−30] Others are readily made via metathesis reactions of arylsodium, aryllithium, or aryl Grignard reagents with PX_3, where X can be a halide, phenoxide, or

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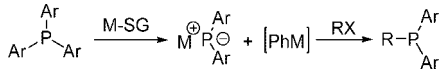
10.1021/ol900222v CCC: $40.75
Published on Web 03/18/2009

alkoxide.[31] Reductive cleavage of triarylphosphine is the most used but can be hard to run and especially to scale up since it requires sodium dispersions in oil.[32,33] Classic metal ammonia reduction introduces problems of handling, over-reduction and operational safety. Solutions of Na−naphthalide have been effective in preparing unsymmetrical diphosphines.[34] However, the presence of coreagents and/or impurities that arise from these routes can introduce challenges in isolation, purification, and subsequent reactions.[35]

Alkali metals absorbed in porous silica gel[36,37] provide an alternative reagent that is nonpyrophoric in dry air, a free-flowing dry powder, and free of contamination by oily hydrocarbons or ammonia. Herein, we report a new method for preparation of diaryl phosphide salts of alkali metals that uses triarylphosphine and alkali metal absorbed in silica gel. The clean diarylphosphide solution thus generated can be decanted and used for subsequent reactions. We report here on comparisons of sodium vs sodium−potassium alloys and the effects of solvents and additives such as ethylenediamine. The method's versatility is tested with various electrophile−triarylphosphine pairings to form substituted diarylphosphines. These monoalkylated phosphines can be further functionalized in a subsequent step to afford aryldialkylphosphines. This approach conveniently accesses substituted phosphines while avoiding transition metals such as Pd or Ni used to mediate couplings.[38]

The conditions for cleavage of triarylphosphines to diaryl phosphides were investigated by using triphenylphosphine as a model substrate. Cleavage of the aryl C−P bond was found to occur under ambient conditions in ether solvents such as THF and dimethoxyethane (DME) at room temperature with 2.5 equiv or more of Na−SG(I) and Na_2K−SG(I). The aryl metal (e.g., phenyl sodium or phenyl potassium) carbanion is formed initially but does not survive under the reaction conditions. Traces of electrophile functionalized aryl compounds were seen in a few midreaction samples (Scheme 1) but never at reaction completion. If need be, however,

Scheme 1. Reductive Cleavage of Triarylphosphine To Generate Diarylphosphide

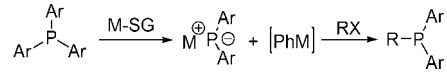


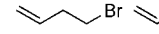
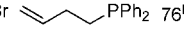
decomposition of the Ar−M (M = Na or K) species can be ensured by brief warming of the reaction mixture to 40−50 °C. In contrast, the cleavage of triarylphosphine with lithium metal gives phenyl lithium and lithium diphenyl phosphide. Phenyl lithium in THF is long lived and has to be quenched with *tert*-butyl chloride at a lower temperature in an additional step.[39] The alkali metal (Na or K) diarylphosphide salt solutions can be quenched in situ or first decanted or filtered under inert atmosphere to remove the M−SG solids and then quenched. Quenching with alkyl halides gave alkyldiarylphosphines in good to high yields (for example, 1-bromobutane yielded *n*-butyldiphenylphosphine in 77% yield).

Cleavage occurred faster in 1,2-DME than in THF and faster with Na_2K−SG(I) than with Na−SG(I). Reaction with Na−SG(I) was, however, accelerated by addition of catalytic ethylenediamine (EDA), finishing in 3 h vs the 6 h required in its absence. The blue color seen in these reactions before phosphine addition suggests formation of Na^- ions in solution, presumably balanced by the EDA−Na^+ complex. The faster rates seen when EDA is added to Na−SG(I) and when Na_2K−-SG(I) was used in place of Na−SG(I) hint at a two-electron transfer from Na^- as opposed to sequential SET steps from elemental Na. Indeed, addition of 18-crown-6, a complexant known to form sodide with Na metal, led to similar accelerations.[40]

The scope of this reaction was studied with different aryl substituents and electrophiles as summarized in Table 1. The

Table 1. Preparation of Monosubstituted Diarylphosphines from Triarylphosphine[a]



entry	PAr_3	electrophile	product	yield or convn (%)
1	PPh_3	^{n}BuBr	^{n}BuPPh$_2$	77[b]
2	PPh_3	TMSCl	TMSPPh$_2$	80[a]
3	PPh_3	MeI	MePPh$_2$	75[a]
4	PPh_3	CyBr	CyPPh$_2$	70[b]
5	PPh_3	C_6F_6	$C_6F_5PPh_2$	70[c]
6	PPh_3	4-Iodo-tol	(4-tol)PPh$_2$	67[c]
7	P(4-tol)$_3$	^{n}BuBr	^{n}BuP(4-tol)$_2$	74[b]
8	P(3,5-xylyl)$_3$	^{n}BuBr	^{n}BuP(3,5-xylyl)$_2$	77[b]
9	P(4-F-Ph)$_3$	^{n}BuBr	^{n}BuP(4-F-Ph)$_2$	0[a]
10	P^{n}Bu$_3$	MeI	No reaction	0[a]
11	PPh_3			76[b]

[a] In all cases, 2.5−3 equiv of Na_2K−SG(I) was used at room temperature in THF unless mentioned otherwise.[41] [b] Conversion measured by ^{31}P NMR. [c] Isolated yield obtained from the quench of the electrophile in same pot. [d] Isolated yield from the decanting of PPh_2^- and quenching with electrophile in a separate flask.

diphenyl phosphide product reacts cleanly with both aliphatic and aromatic halide electrophiles (entries 1−6). The reductive cleavage takes place with more electron-rich phosphines such

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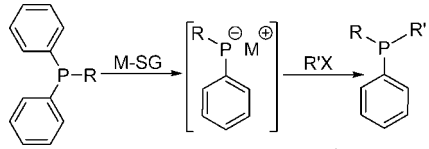
as tris(*p*-tolyl)phosphine and tris(3,5)xylylphosphines, but at a slower rate (entries 7 and 8). With tris(*p*-fluorophenyl)phosphine (entry 9), even a modest excess of Na_2K−SG(I) and longer reaction time yielded only defluorination products, and an 18-fold excess led to diphenyl phosphide, as expected from plain triphenylphosphine cleavage. No reaction was seen with tributylphosphine (entry 10).

Quenching of the diphenyl phosphide with butyl or homoallyl bromides achieved monofunctionalization in good yield (entries 1 and 11), but activated electrophiles such as benzyl and allyl bromides formed quaternary salts.

Next, we looked at cleavage reactions of monoalkyldiarylphosphines to see if we could further functionalize them. The targets would be phosphines bearing three different substituents and, hence, chiral (albeit racemic). Interestingly, alkyldiarylphosphines underwent cleavage losing an aryl ring to afford the corresponding alkyl aryl phosphide solutions. However, dialkylarylphosphines resist cleavage completely.

Understanding the factors controlling selectivity in the cleavage of alkyldiarylphosphines may allow design and control of stereochemistry and redox potentials of organometallic complexes.[42] Such reactions have been studied[43] but mostly in the context of P-arylated bisphosphines with varying spacers.[44−49] For cleavage of the simpler butyldiphenylphosphine, we find nearly exclusive dearylation to form butyl phenyl phosphide (Scheme 2). This result seems

Scheme 2. Reductive Cleavage of Diarylalkylphosphine to Tertiary Phosphines



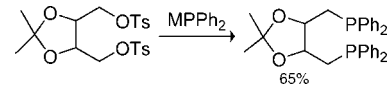
a R = R' = ^{n}Bu = 68%
b R = ^{n}Bu R' = Cy = 89%

sensible in terms of the relative stabilities of phenyl vs butyl carbanion salts (pK_a(R−H) ∼ 43 and 50, respectively[50]), assuming they are formed directly in the cleavage. However, since alkyl−H bond dissociation energies are typically 5−15 kcal/mol lower than aryl−H, if the severed group departed as a radical, diaryl phosphide formation might be expected. This latter process may explain the previously reported selective cleavage[26] of trimethylsilyldiphenylphosphine to form diaryl phosphide, a result we have confirmed as well.

Scheme 2 above summarizes results of cleavage with subsequent alkylation to form nonsymmetric phosphines. These reactions could be carried out via two sequential dearylation/alkylation cycles in one pot without the need for isolation of the intermediate monoalkylated phosphines. As long as sufficient M−SG was added in the second cycle, no difficulties arose due to the presence of slight excesses of alkyl halide quenchers such as 1-bromobutane and bromocyclohexane. Overall, product yields were between 68−89%. This approach did not, however, extend to a third cycle; like their trialkyl congeners, the dialkylarylphosphines (e.g., Et_2PPh) did not undergo any detectable cleavage reactions with M−SG reagents.

Finally, as an illustration of its synthetic utility, this new method was used to make the chiral ligand DIOP [2,2-dimethyl-4,5-bis(diphenylphosphinomethyl)dioxolane] (Scheme 3). DIOP is used widely as a ligand for asymmetric versions

Scheme 3. Preparation of DIOP from Diaryl Phosphide Solution



65%

of hydroformylation,[51] hydrogenation,[52−59] allylic alkylation,[60] radical addition, and polymerization[61] reactions. This is an attractive ligand as it can be directly accessed from tartaric acid via acetal formation, esterification, reduction with $LiAlH_4$ and activation by tosylate formation. The final step involves a nucleophilic displacement of $^-$OTs by $^-PPh_2$. K_2Na alloy has been used for this purpose in synthesis.[62−64]

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Here, we have shown the ability of the more convenient and less hazardous $Na_2K-SG(I)$ reagent to effect the same reaction in comparable yields.

To summarize, alkali metals absorbed in silica gel have been shown to be efficient reagents for carrying out the cleavage and derivatization of di- and triarylphosphines. The diaryl and alkyl aryl phosphides that this method cleanly generates are useful as reagents and as building blocks for modified arylphosphine ligands.

Acknowledgment. We thank Dr. Daniel Holmes of Michigan State University's NMR facilty for invaluable assistance with ^{31}P NMR experiments. The Dreyfus foundation's support of P.B.'s undergraduate research via a Senior Scientist Mentor award to J.L.D. and funding from SiGNa Chemistry, Inc. for P.N.'s graduate assistantship are also gratefully acknowledged.

Supporting Information Available: Experimental procedures and NMR data from these studies. This material is available free of charge via the Internet at http://pubs.acs.org.

OL900222V

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