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Radical-based reduction of phosphine sulfides and phosphine selenides by $(Me_3Si)_3SiH$

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Abstract

Tris(trimethylsilyl)silane reacts with phosphine sulfides and phosphine selenides under free radical conditions to give the corresponding phosphines in good yields. Stereochemical studies on P-chiral phosphine sulfides show these reductions proceed with retention of configuration.

Keywords: phosphine sulfides; reduction; radical reactions.

In recent years radical reactions have proven to be valuable in organic synthesis. The selective removal of functional groups or atoms to generate carbon-centered radicals and the formation of carbon–carbon bonds has been the workhorse for those who employ radical chemistry in synthesis of complex molecules.[1] Furthermore, great progress in the stereoselective control of radical reactions has also been accomplished.[2] On the other hand, the radical chemistry associated with functional groups attached to atoms other than carbon has received much less attention. In this communication, we report preliminary results concerning a novel radical chain reduction of phosphine sulfides and phosphine selenides to the corresponding phosphines as well as the stereochemical outcome.

We reasoned that $(Me_3Si)_3SiH$[3] could have the right properties to achieve the reduction of phosphine sulfides and phosphine selenides by a radical chain reaction based on the following observations: (i) In view of the affinity of silyl radicals for sulfur and selenium atoms,[4] the addition of the $(Me_3Si)_3Si^{\bullet}$ radical to the P=X double bond to give a phosphoranyl intermediate **1** is expected to be a facile process (Scheme 1).

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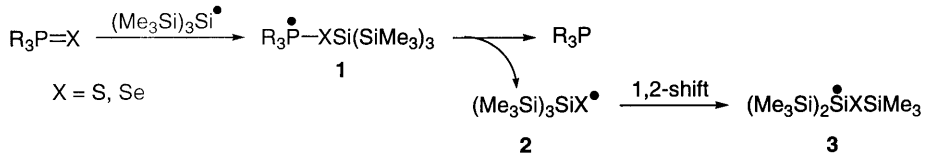
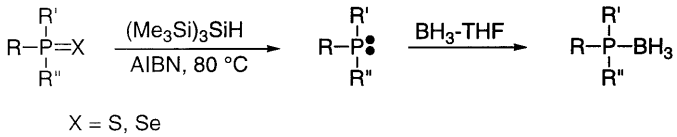


Scheme 1.

(ii) The α-fragmentation of phosphoranyl radicals is well documented[5] and radical **1** is likely to undergo this path for certain R substituents. (iii) The formed sulfur-centered radical **2** is known to undergo an efficient 1,2-shift of the Me_3Si group from the silicon to the sulfur atom to give radical **3**.[4,6] Hydrogen abstraction from the silane should regenerate the $(Me_3Si)_3Si^{\bullet}$ radicals, thus completing the cycle of a chain reaction.[7,8]

The feasibility of reduction with $(Me_3Si)_3SiH$ was tested using triphenyl phosphine sulfide and triphenyl phosphine selenide. The reactions of $Ph_3P{=}S$ or $Ph_3P{=}Se$ with an equimolar amount of $(Me_3Si)_3SiH$ in toluene at 80°C in the presence of AIBN as the radical initiator gave crystalline Ph_3P in 96% yield. On the other hand, treatment of the resulting crude mixture with 1 equiv. of BH_3–THF afforded the corresponding stable phosphine–borane complex in 90% yield (Scheme 2 and Table 1). The reaction was still efficient with n-$Bu_3P{=}S$ and n-$Bu_3P{=}Se$, although longer reaction times and higher concentrations of the reducing agent were required. In the case of mixed alkyl and aryl substituted phosphine sulfides, intermediate reactivities were observed (Table 1). It is also worth mentioning that the reactions with $Ph_3P{=}O$ and n-$Bu_3P{=}O$ were unsuccessful, even at temperatures as high as 150°C.



Scheme 2.

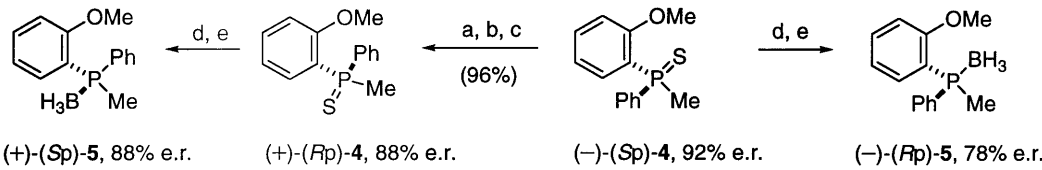
Table 1
Reaction of RR′R″P=X with $(Me_3Si)_3SiH$

RR′R″P=X	Time (h)/equiv. $(Me_3Si)_3SiH$[a]	RR′R″P, yield (%)	RR′R″P–BH_3, yield (%)[d]
n-$Bu_3P{=}S$	5/3	–	75
Met-BuPhP=S	5/1	90[c]	88
MePhArP=S[b]	3/1	–	96
$Ph_3P{=}S$	1/1	96[d]	90
n-$Bu_3P{=}Se$	6/3	–	75
$Ph_3P{=}Se$	2/1	96[d]	–

[a] Reaction conditions: 0.2 M of RR′R″P=X and AIBN (10 mol%) in deoxygenated toluene at 80°C.
[b] Ar = o-MeO–C_6H_4.
[c] ^1H NMR yields using $(PhCH_2)_2O$ as internal standard.
[d] Isolated yields after solvent evaporation and flash chromatography of the crude reaction mixture.

For the purpose of stereochemical studies, (–)-(*S*p)-*o*-anisylphenylmethylphosphine sulfide (**4**) was prepared by the Corey protocol.[9] Furthermore, the (–)-(*S*p)-**4** enantiomer (92% e.r.) was converted into the opposite (+)-(*R*p)-**4** (88% e.r.)[10,11a] in a three-step procedure and in 96%

overall yield as follows: (a) Stereoretentive oxidation of (–)-(*S*p)-**4** with OXONE® into the corresponding phosphine oxide.[12] (b) Reduction of the phosphine oxide with Cl_3SiH in the presence of Et_3N to phosphine, according to Horner and Balzer with inversion of configuration at the phosphorus center.[13] (c) Oxidation of the phosphine with elemental sulfur with retention of configuration (Scheme 3).[14]



Scheme 3. Reagents and conditions: 2 equiv. OXONE, THF, 2 h; (b) 5 equiv. Cl_3SiH, 5 equiv. Et_3N, PhH, 80°C, 3 h; (c) 1 equiv. S_8, PhH, 80°C, 3 h; (d) $(Me_3Si)_3SiH$, AIBN, PhH, 80°C, 3 h; (e) BH_3–THF, rt, 2 h

Each enantiomer **4** was treated separately with $(Me_3Si)_3SiH$ under the conditions elaborated earlier for analogous racemic compounds (Table 1) and the enantiomeric phosphines were isolated and analyzed as stable BH_3 complexes **5**.[9,11b] The conversion of (+)-(*R*p)-**4** into (+)-(*S*p)-**5** was stereoselective whereas the reduction of (–)-(*S*p)-**4** afforded (–)-(*R*p)-**5** with some decrease of enantiomeric purity in 3 h (Scheme 3). When these reactions were interrupted after 1.5 hours (at ca. 50% of the consumption of the starting material), both of them were stereospecific, which indicates some epimerization by secondary processes occurring in the full-time reaction of (–)-(*S*p)-**4**. A detailed study on the stereospecificity of these reactions is in progress.

The reduction of phosphine sulfides to the corresponding phosphines is of general interest, since today P-chiral phosphines play a fundamental role in the development of enantioselective transition metal catalysts[15] and phosphine sulfides can be considered as the safe and stable precursors thereof. So far, the most effective method of reduction of P-chiral phosphine sulfides relies on the use of hexachlorodisilane as developed by Mislow and co-workers.[16] However, our radical method achieves comparable stereochemical outcomes using milder conditions and therefore is recommended for sensitive substrates.

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10. (*S*p) and (*R*p) refer to the configuration at phosphorus and e.r. refers to the enantiomeric ratio.
11. Analytical conditions: (a) HPLC, 25 cm chiral column Chiralpack AD, eluent: *i*-PrOH/hexane (20:80), flow 0.7 mL/min.; elution times: (−)-(*S*p)-**4** at 12.1 min, (+)-(*R*p)-**4** at 15.18 min. (b) HPLC, 25 cm Chiral Daicel OJ column, eluent: *i*-PrOH/hexane (40:60), flow 0.7 mL/min; elution times: (−)-(*R*p)-**5** at 22.0 min, (+)-(*S*p)-**5** at 39.4 min.
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