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Reductive conversion of phosphoryl P(O) compounds to trivalent organophosphines R_3P

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ABSTRACT

By introducing trimethylsilyl chloride (TMSCl), the pentavalent phosphoryl P(V) compounds such as triphenylphosphine oxides, secondary phosphine oxides etc., were readily converted to the corresponding $R_2P(OTMS)$ intermediates, that can further react efficiently with an electrophile R'X or with a nucleophile R'Li to produce the corresponding trivalent phosphines R_2PR'. Chiral phosphines could also be obtained stereospecifically by this strategy.

Introduction

Triphenylphosphine oxide $Ph_3P(O)$ is a well-known chemical waste generated from the Wittig reactions etc. that are widely used in organic synthesis and industry for the preparation of highly valuable compounds such as Vitamin A [1]. Tens of thousands tons of $Ph_3P(O)$ are generated every year, and a large portion of them have to be discarded as useless chemical waste because of the limited utilities [2]. This situation has been a big concern for more than half a century. To solve this problem, extensive studies on $Ph_3P(O)$ are carried out world widely [3].

We have recently reported that, sodium is superior to lithium and potassium, that can efficiently convert $Ph_3P(O)$ and related organophosphorus compounds easily and efficiently, by cleaving a Ph-P bond, to other phosphoryl P(O) compounds $Ph_2P(O)R$ etc. (R = H, alkyl and aryl groups), providing a new general and economic way for transforming P(V) compounds to other P(V) compounds (Scheme 1A) [4]. During these investigations, we also noted that, occasionally, a small amount of trivalent phosphine Ph_2PR could be also observed as a side product. This phenomenon greatly attracted our attention because it unusually indicates that, *from this disposed waste $Ph_3P(O)$, we can not only produce the pentavalent phosphoryl compounds $Ph_2P(O)R$, but may also produce the more valuable trivalent phosphine Ph_2PR* that possesses a central position in organic synthesis and organometallic chemistry [5]. Of course, in the laboratory, Ph_2R may be produced from Ph_2PCl and RM (M = Li, MgX) (eq 1). However, chlorophosphines are expensive and difficult to handle. Beyond the economic advantage, this shows a new way for converting $R_3P(O)$ compounds to trivalent phosphines R_3P, as the known conventional methods predominantly use a hydride reducing reagent such as $LiAlH_4$ etc. in order to remove the oxygen on P(O) (eq 1) [3,6].

$$Ph_2PCl \xrightarrow[M = Li, MgX]{RM} Ph_2PR \xleftarrow{LiAlH_4,\ HSiR_3\ etc.} Ph_2P(O)R \quad (1)$$

Herein, we communicate that by introducing TMSCl to the $Ph_3P(O)$/Na reaction system, diphenyl(trimethylsiloxy)phosphine $Ph_2P(OTMS)$ can be generated that react efficiently further with an electrophile (path a) or with a nucleophile (path b) to produce the desired Ph_2PR (Scheme 1B). The reaction can be carried out one-pot by sequentially adding the required chemicals starting from $Ph_3P(O)$, thus providing a convenient way for directly converting $Ph_3P(O)$ to Ph_2PR. This strategy can be applied to a variety of phosphoryl compounds, showing this is a general way for reductively converting a pentavalent P(V) phosphoryl compound to the corresponding trivalent P(III) organophosphines R_3P. It was noted that, to the best of our knowledge, the present strategies are surprisingly totally unprecedented to date [7].

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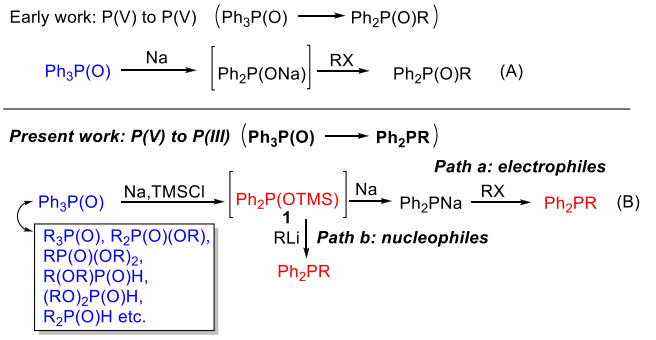
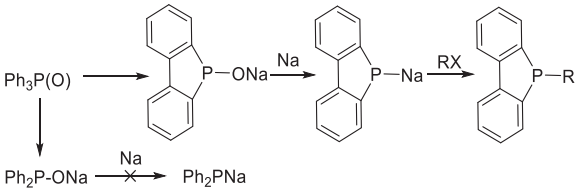


Scheme 1. Conversion of $Ph_3P(O)$ using sodium to $Ph_2P(O)R$ and Ph_2PR. (A): P(V) to P(V); (B): P(V) to P(III).

Results and discussion

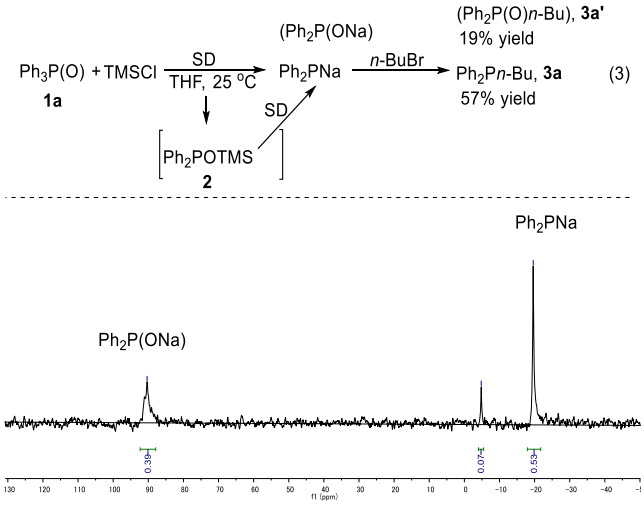
We have found that the trivalent dibenzophospholes can be generated by a mild reduction with sodium via sequential reactions starting from $Ph_3P(O)$ (eq 2) [3b]. Therefore, we initially thought that Ph_2PONa might also be similarly reduced to Ph_2PNa by sodium (SD: sodium dispersed in paraffin with μm-scale particles). However, disappointedly, contrary to our expectation, we found that Ph_2PONa could hardly be reduced to Ph_2PNa even under heating at an elevated temperature for a long time in the presence of a large excess amount of SD.



(2)

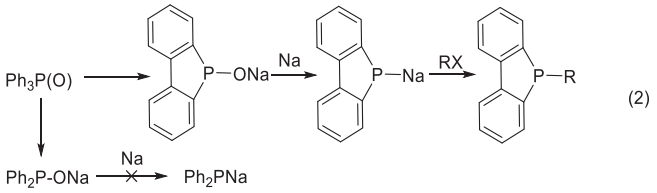
Since Na alone is not able to reduce Ph_2PONa to Ph_2PNa, we then added an additive to the reaction system that might act as an "activator" to "activate" Ph_2PONa so that it could be reduced to Ph_2PNa. Many such "activators" were then tested, and finally we noted that when TMSCl was introduced to the reaction system, the corresponding Ph_2Pn-Bu was detected (eq 3)! Thus, to a mixture of $Ph_3P(O)$ (0.25 mmol) and TMSCl (0.50 mmol) in THF (2 mL) was added SD (0.50 mmol) at room temperature. The color of the solution gradually changed from grey to black and then orange, after stirring the mixture for 4 h. The precipitates were removed by centrifugation and ^{31}P NMR spectroscopy showed that Ph_2PNa (δ_p = −19.6 ppm) was generated (Scheme 2). Then *n*-BuBr (0.5 mmol) was added to the transparent solution and Ph_2Pn-Bu (δ_p = -15.8 ppm) was obtained in 57% yield based on $Ph_3P(O)$ used as estimated by ^{31}P NMR spectra (Fig. S1). The product $Ph_2P(O)n$-Bu (δ_p = 28.7 ppm) *via* $Ph_2P(ONa)$ (δ_p = 90.3 ppm) was also generated in 19% yield. Then, efforts were devoted to improving the yield of Ph_2Pn-Bu (Table 1). However, only 72% yield of **3a** could be achieved (run 1).

Carefully analyzing the reaction paths for the formation of Ph_2PNa in eq 3, we realized that Ph_2POTMS perhaps was the reactive intermediate because $Ph_2P(ONa)$ generated from $Ph_3P(O)$ with sodium could be readily trapped by TMSCl. This speculation was correct as confirmed by a separate experiment by employing the isolated $Ph_2P(OTMS)$, and Ph_2Pn-Bu could be obtained in a quantitative yield (eq 4)!



Scheme 2. Reduction of $Ph_3P(O)$ to Ph_2PNa.

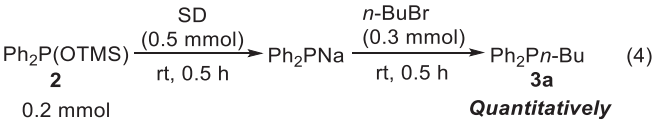
Table 1
Reaction conditions optimization.[a]



(2)

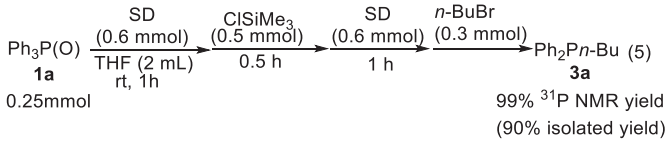
run	SD	TMSCl	Yield of **3a**/**3a'**
1	4 equiv	2 equiv	72%/22%
2	6 equiv	2 equiv	62%/17%
3	8 equiv	2 equiv	69%/15%
4	4 equiv	1 equiv	33%/67%
5	4 equiv	3 equiv	42%/39%

[a] Reaction condition: $Ph_3P(O)$ **1a**, (0.25 mmol), THF (2.0 mL), TMSCl (0.25–0.75 mmol), SD (1.0–2.0 mmol), rt, 4 h. After filtration, *n*-BuBr (0.5 mmol), rt, 0.5 h. Yields refer to ^{31}P NMR yields based on **1a** used.

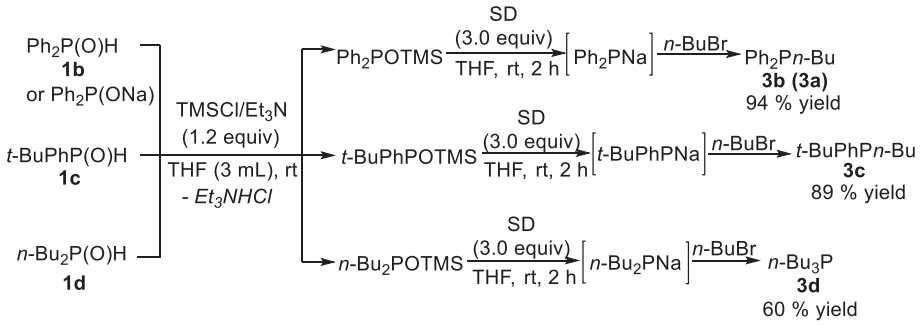


(4)

Having verified that $Ph_2P(OTMS)$ was the real active intermediate for the conversion of $Ph_3P(O)$ to Ph_2Pn-Bu, we can conduct a one-pot reaction starting from $Ph_3P(O)$ more efficiently without isolating $Ph_2P(OTMS)$. Thus, as shown in eq 5, $Ph_3P(O)$ reacted with sodium to generate $Ph_2P(ONa)$ first. To this mixture was then added TMSCl to in situ give $Ph_2P(OTMS)$. Sodium was then added to generate Ph_2PNa which was trapped by *n*-BuBr to give Ph_2Pn-Bu in 90% yield!



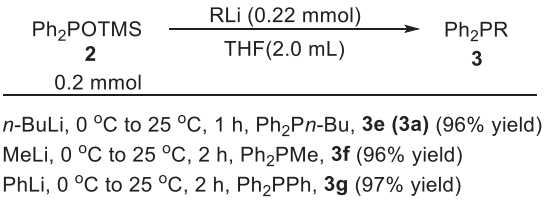
(5)



Scheme 3. Efficient P-OTMS bond cleavage of $R_2P(OTMS)$ by sodium generating R_2PNa.

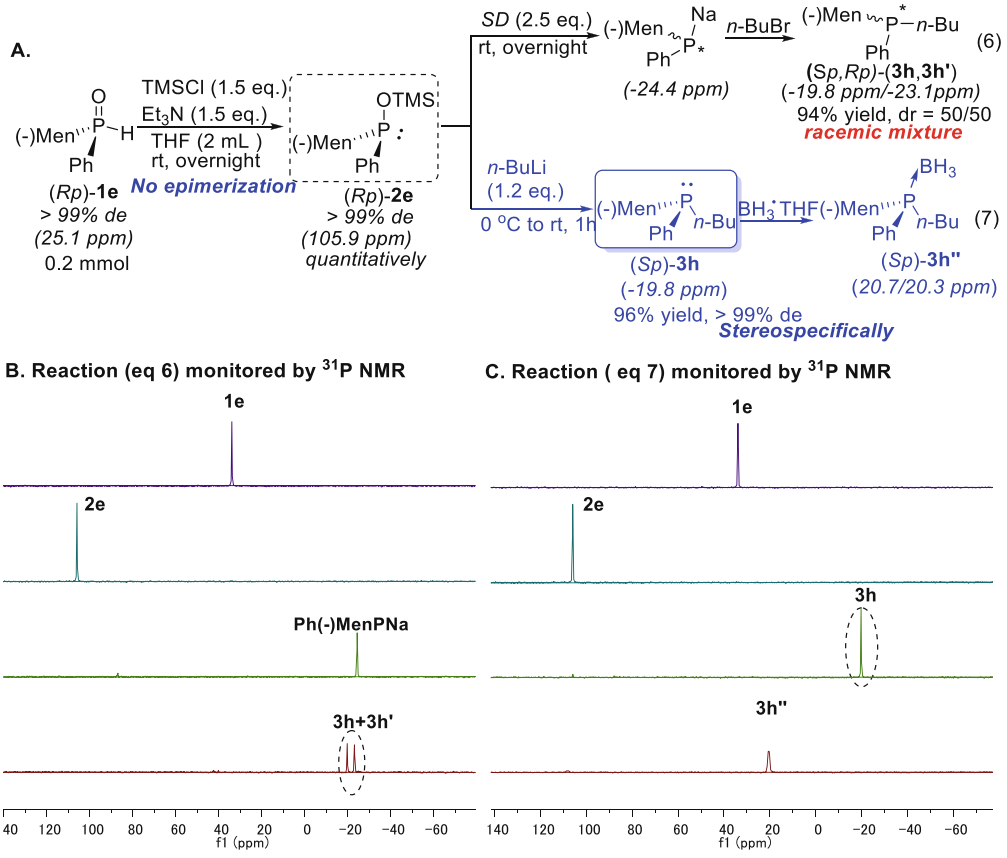
As could be readily expected, by using this strategy, other secondary phosphine oxides $R_2P(O)H$ could be also readily reductively converted to the corresponding trivalent phosphines (Scheme 3).

A further study on the reactivity of $Ph_2P(OTMS)$ fantastically revealed that the OTMS unit can be replaced easily by RLi via a nucleophilic substitution reaction, remarkably demonstrating that $Ph_2P(OTMS)$ can act like "an ambiguous reagent" that both an electrophile and an nucleophile can be used for converting $Ph_2P(OTMS)$ to Ph_2PR (Scheme 1)! For example, $Ph_2P(OTMS)$ in THF rapidly reacted with *n*-BuLi at 0 °C to produce Ph_2Pn-Bu in 96% yield (Scheme 4). In addition, MeLi and PhLi could also be used as efficient nucleophiles to react with $Ph_2P(OTMS)$, to give the substitution product Ph_2PMe and Ph_3P in 96% and 97% yield, respectively.



Scheme 4. Efficient substitution reactions of $Ph_2P(OTMS)$ with RLi generating Ph_2PR.

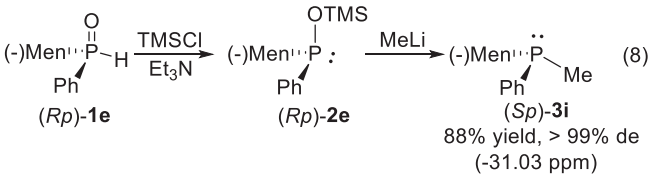
Very importantly, this substitution reaction can be used for the preparation of the highly valuable chiral phosphines that are quite difficult to prepare by other methods despite its high value. We have developed an efficient way for the preparation of chiral-P(O) compounds [8]. As demonstrated in Scheme 5, we first confirmed that a chiral-P(O)H compound (*Rp*)-**1e** (s, δ_p = 25.1 ppm) can readily be changed to the corresponding (*Rp*)-(-)MenPhPOTMS **2e** (s, δ_p = 105.9 ppm) (B). No epimerization took place at all, and the stereochemistry retained at the phosphorus center! Treatment



Scheme 5. Preparation of chiral-phosphines via the reaction of (*Rp*)-(-)MenPhP(O)H with SD or *n*-BuLi monitored by ^{31}P NMR.

of the (*Rp*)-**2e** with 2.5 equivalents of SD at room temperature and subsequent quenching with *n*-BuBr resulted in the racemic mixture of (*Sp*,*Rp*)-(-)MenPhP*n*-Bu (**3h**/**3h'**) (d, δ_P = −19.8/−23.1 ppm), albeit with high yield (eq 6). Secondly, and excitingly, the substitution with RLi took place stereospecifically. Thus, to the POTMS solution was dropwise added 1.2 equivalents of *n*-BuLi at 0 °C and stirring for 1 h, only one signal appeared at −19.8 ppm as confirmed by ^{31}P NMR, indicating that (*Sp*)-(-)MenPhP*n*-Bu **3h** was generated stereospecifically in a high yield (eq 7). Protection with BH_3·THF afforded the air-stable P-B compound **3h''** (d, 20.5 ppm, $J_{B\text{-}P}$ = 64.8 Hz) that was characterized by ^{1}H and ^{13}C NMR (SI) [9a].

Using the same strategy, MeLi could also efficiently react with (*Rp*)-**2e** with inversion of configurations at phosphorus to give the stereospecific product (*Sp*)-(-)MenPhPMe in 88% yield (eq 8) [9b].



(8)

Conclusions

In summary, we have developed a TMSCl/Na reduction strategy for the conversion of pentavalent phosphoryl compounds to trivalent phosphines. This method completed our on-going studies on the utilization of $Ph_3P(O)$, showing that from $Ph_3P(O)$ not only $Ph_2P(O)R$ but also Ph_2PR could be produced via the key Ph_2P(OTMS) intermediate. In addition, the highly valuable chiral-phosphines can also be easily generated stereospecifically from the corresponding phosphine oxide by using this new strategy.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.tetlet.2021.152870.

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