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Synthesis of Phosphinines

Reduction of λ⁵-Phosphinines

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Abstract: A convenient method to easily prepare parent λ³-phosphinine from easily accessible λ⁵-precursors was developed. A series of λ⁵-phosphinines bearing heteroatom substituents OMe, SMe, and/or NMe_2 at the phosphorus atom were prepared by electrocyclization of phosphahexatrienes generated in situ. Reaction conditions for the synthesis of λ⁵-phosphinines were optimized. The molecular structure of 1,1-dimethoxy-λ⁵-phosphinine was determined by an X-ray diffraction analysis. A series of reducing agents were tested in order to prepare λ³-phosphinine. 1,1-Dimethoxy-λ⁵-phosphinine was reduced by $LiAlH_4$. The method of choice appeared to be the reduction of bis(dimethylamino)-λ⁵-phosphinine with diisobutylaluminium hydride (DIBAL-H) in 30 % overall yield starting from vinyl ethyl ether.

Introduction

Even after half a century after the publication by Märkl[1] on the synthesis of the first stable λ³-phosphinine, many of these compounds remain accessible only with difficulty. This is especially true for the parent λ³-phosphinine prepared by Ashe[2] and phosphinines featuring basic functional groups. Methods for the synthesis and properties of phosphinines are well-documented.[3] Two main methods for functionalized phosphinines have been developed so far. The first one is based on the reaction of pyrylium salts with phosphine or its equivalents.[4] The method is well-developed, but provides access to 2,4,6-substituted derivatives. The second method is the reaction of 1,3,2-diazaphosphinines with disubstituted alkynes through a cycloaddition/cycloreversion sequence.[5] Both methods have limited opportunities for varying substitution patterns. Other syntheses of functionalized phosphinines are considered as milestones, for example, those of 2-hydroxyphosphinine[6] and aldehyde phosphinine.[7] Among the latest approaches to λ³-phosphinines, an iron-catalyzed [2+2+2] cycloaddition reaction of diynes with phosphaalkynes should be mentioned.[8]

λ³-Phosphinines can be prepared by reduction of the corresponding λ⁵-phosphinines.[9] Nevertheless, the approach is not considered as a practical one, as λ⁵-phosphinines are mainly synthesized from λ³-phosphinines.

Previously we have shown that λ⁵-phosphinines can easily be prepared by starting from common building blocks by electrocyclization of variously substituted hexaphosphatrienes.[10] The procedure allows synthesis of both parent and highly substituted phosphinines. All λ⁵-phosphinines synthesized have aryl, alkyl, dialkyl amino substituents or a mixture of those substituents at the phosphorus atom.

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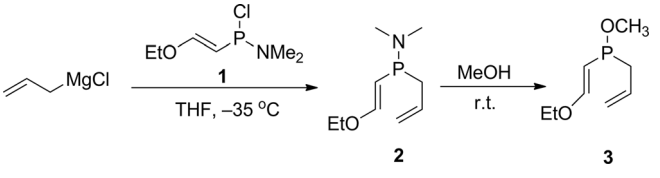
Analogous electrocyclization of hexaphosphatrienes featuring a trivalent phosphorus atom was also attempted. Mathey et al. have demonstrated that flash vacuum pyrolysis (FVP) of tris(allyl)phosphane or vinyl(diallyl)phosphane gave phosphinines probably via hexaphosphatrienes.[11] An attempt to prepare phosphahexatrienes featuring trivalent phosphorus or their metal complexes did not produce the targeted λ³-phosphinines.[12]

In the literature, synthesis of λ³-phosphinines was described by reduction of λ⁵-phosphinines featuring dimethoxy groups at the phosphorus atom.[9] Thus, reduction of λ⁵-phosphinines to λ³-phosphinines might be a solution, provided they are readily available by an alternative route. In this work we describe the synthesis of λ⁵-phosphinines featuring OMe, SMe, and/or NMe_2 groups at the phosphorus atom and their reduction into parent λ³-phosphinine.

Results and Discussion

1.1. Synthesis of λ⁵-Phosphinines

Amide **2** was prepared by slow addition of chlorophosphine **1** into a solution of allylmagnesium chloride in THF with vigorous stirring (Scheme 1). Phosphinite **3** was obtained upon treatment of amide **2** with methanol at room temperature.



Scheme 1. Synthesis of amide **2** and phosphinite **3**.

All compounds bearing 2-ethoxyvinyl groups, for example **1**, **2**, **3**, **4a**–**c**, exist predominantly as *trans*-isomers, but *cis*-isomers (ca. 2 %) are also present as evidenced by ^{1}H and ^{31}P NMR spectra. Signals of all *cis*-isomers in ^{31}P NMR spectra are 3.6–

9.1 ppm upfield with respect to *trans*-isomers. Compounds **2** and **3** were oxidized with a hydrogen peroxide urea complex, elemental sulfur or selenium giving air-stable distillable compounds **4a**–**d** (Scheme 2).

Alkylation of compounds **4a**–**d** with methyltriflate was accomplished at –70 °C in dichloromethane. Salts **5a**–**d** are air-sensitive viscous oils. In their ^{1}H NMR spectra, a distinctive pattern of allyl methylene protons with $J_{P,H}$ coupling constant values ranging from 18.3 Hz for **5b** to 61.0 Hz for **5c** and 100.8 Hz for **5d** was observed. In their ^{31}P NMR spectra, the signals of phosphonium salts ranged from δ = 77.1 ppm for **5a**, δ = 68.2 ppm for **5b**, δ = 70.5 ppm for **5c**, and δ = 64.4 ppm with a coupling constant of $^1J_{PSe}$ = 467 Hz for **5d**.

In a previous work, electrocyclization of phosphahexatrienes to prepare λ^5-phosphinines in situ by deprotonation of phosphonium salts with *n*-butyllithium was established quite well by some of us.[10a]

In order to optimize the reaction conditions and maximize the yield of λ^5-phosphinines (Scheme 3), we tested different bases and varied some other reaction conditions (Table 1).

It was found that LiHMDS is a universal base: it gave symmetric and unsymmetric phosphinines in moderate to good yields (entries 1, 6, 7, 8), while *t*BuOK worked well only with phosphonium salt **5e**, which has bis(dimethylamino) groups at the phosphorus atom (entry 9). The reaction requires at least 2 equiv. of the base and should be carried out at low temperature. When only 1 equiv. of LiHMDS was used, the yield dropped markedly (entry 3). Also we found that in the phosphine synthesis the more concentrated the solution, the lower were the yields (entry 11). This is probably due to polymerization of phosphahexatrienes.

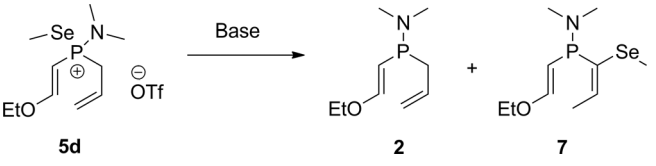
All λ^5-phosphinines **6a**–**c**,**e** are air-stable compounds, which slowly darken upon storage even under argon. In ^{31}P NMR spectra, signals of phosphinines are upfield with respect to the corresponding phosphonium salts.

Table 1. Reaction conditions for the deprotonation of phosphonium salts **5a**–**c**,**e** and yields of the corresponding phosphinines **6a**–**c**,**e**.

Entry	Salt	Base[a]	*T* [°C]	Isolated yield [%]
1	**5a**	LiHMDS	–75	62
2	**5a**	LiHMDS	0	traces[b]
3	**5a**	LiHMDS (1 equiv.)	–75	< 27[b]
4	**5a**	*n*BuLi	–75	26
5	**5a**	*t*BuOK	–70	traces[b]
6	**5b**	LiHMDS	–70	78
7	**5c**	LiHMDS	–80	76
8	**5e**	LiHMDS	–75	67
9	**5e**	*t*BuOK	–70	82
10	**5e**	*t*BuOK	–75	48[c]
11	**5e**	*n*BuLi	–80	26
12	**5e**	*n*BuLi	–78	45[10a]

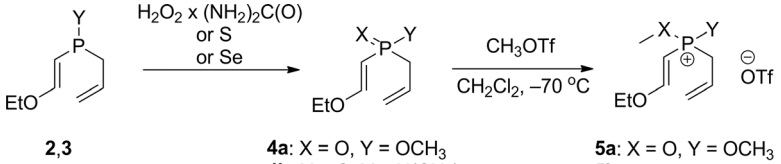
[a] The reaction was carried out in THF, and the ratio of base to phosphonium salt was 2.1:1 unless otherwise specified. [b] Judging by ^{31}P NMR spectroscopy. [c] CH_2Cl_2 was used as a solvent.

Upon treatment with LiHMDS, phosphonium salt **5d** showed totally different chemical properties from those of salts **5a**–**c**,**e** (Scheme 4).

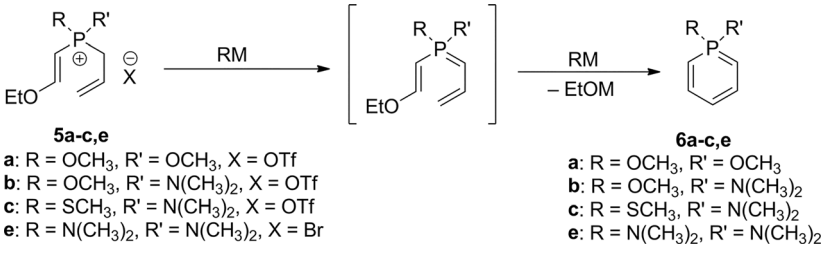


Scheme 4. Deprotonation of phosphonium salt **5d**.

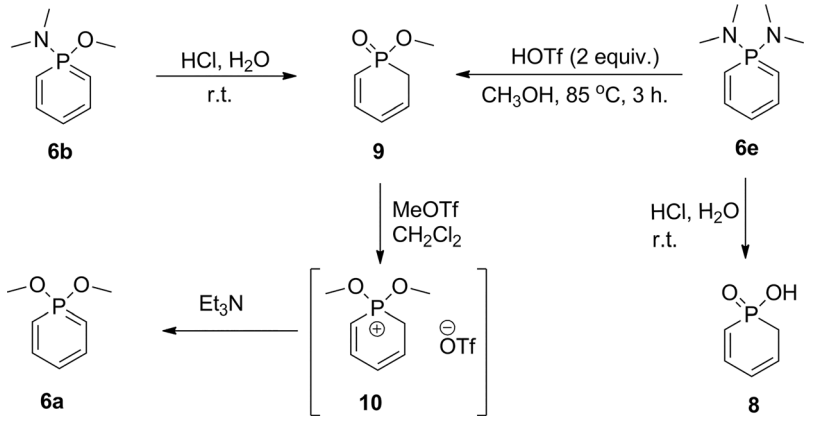
Under these conditions, amide **2** was separated as a major (78 %) product (Table 2, entry 1). Such an observation can be rationalized if LiHMDS is considered as a nucleophile attacking the SeMe group of salt **5d** (Figure S2 in the Supporting Information). In addition, a compound with tentative structure **7** was separated. An opposite tendency was observed when *t*BuOK was employed as a base (Table 2, entry 2).



Scheme 2. Synthesis of phosphonium salts **5a**–**d**.



Scheme 3. Synthesis of phosphinines **6a**–**c**,**e**.



Scheme 5. Interconversions between phosphinines.

Table 2. Deprotonation of phosphonium salt **5d**; composition (%) of the reaction mixture.

Entry	Base	*T* [°C]	**2**	**7**
1	LiHMDS	–80	78	22
2	*t*BuOK	–80	37	63
3	*t*BuOK	–20	59	41

For compound **6a** we were able to grow crystals suitable for single-crystal X-ray diffraction analysis. Recently we reported the X-ray structure of the phosphinine bearing morpholyl groups at the phosphorus atom.[10a] The molecular structure of compound **6a** has been determined by a single-crystal X-ray diffraction analysis. The perspective view of molecule **6a** and selected geometrical parameters are given in Figure 1. The central six-membered cycle is planar within 0.004 Å. It is worth to note that both P1–C1 and P1–C1′ bonds are shortened in comparison with the average value of 1.80 Å for C_{ar}–P^{V}.[13] In **6a** they are both 1.705(2) Å. The C–C bond lengths in the central cycle vary in the narrow range of 1.384(3) to 1.391(3) Å.

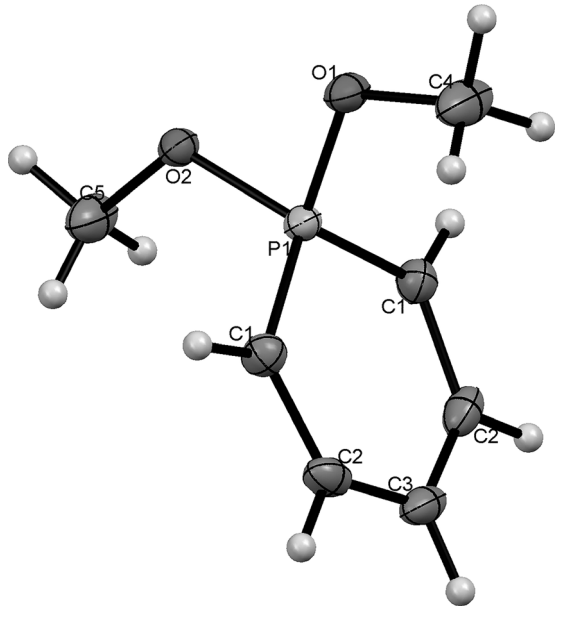


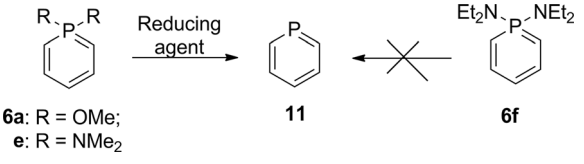
Figure 1. The perspective view of **6a**. Selected bond lengths [Å] and angles [°]: P1–C1′ 1.705(2), P1–O1 1.591(2), P1–O2 1.597(2), P1–C1 1.705(2), C1–C2 1.391(3), C2–C3 1.384(3); C1′–P1–O1 114.61(8), C1′–P1–O2 115.35(8), O1–P1–O2 91.4(1), C1′–P1–C1 105.6(2), O1–P1–C1 114.61(8), O2–P1–C1 115.35(8).

Dimroth showed that under acidic conditions phosphinines could easily exchange substituents at the phosphorus atom or hydrolyze to the corresponding phosphinic acid derivatives.[14] We found that, on being dissolved in concentrated hydrochloric acid, phosphinine **6e** was readily transformed into phosphinic acid **8** (Scheme 5). Under the same conditions, phosphinine **6b** gave phosphinic ester **9**.

Compound **9** was also obtained from **6e** by treatment with trifluoromethanesulfonic acid in methanol. Alkylation of ester **9** with MeOTf probably gave phosphonium salt **10**, which, upon deprotonation with Et_3N, yielded phosphinine **6a**. This provides an alternative route to phosphinine **6a**.

1.2 Reduction of λ⁵-Phosphinines to λ³-Phosphinine

In the literature there are few examples for the reduction of dimethoxy-λ⁵-phosphinines to λ³-phosphinines with various reducing agents.[9] We decided to explore a few commonly available reducing agents for the reduction of λ⁵-phosphinines **6a**,**e** (Scheme 6).



Scheme 6. Reduction of λ⁵-phosphinines **6a**,**e**.

Lithiumaluminium tetrahydride is a convenient reagent for the reduction of dialkyl alkylphosphonates to $RP(O)H_2$ compounds.[15] We successfully applied $LiAlH_4$ in boiling ether for the reduction of phosphinine **6a** (Table 3, entry 1). After work-up, a parent phosphinine, compound **11**, was separated and characterized by its ^{1}H, ^{13}C, ^{31}P NMR spectra,[16] which were identical to those reported previously.

Table 3. Reduction of λ⁵-phosphinines.

Entry	Substrate	Reducing agent	*T* [°C]	Solvent	Yield [%]
1	**6a**	$LiAlH_4$ (1.06 equiv.)	35	Et_2O	15
2	**6a**	$LiAlH_4/Me_3SiCl$ (3.6 equiv.)	35	THF	72[a]
4	**6e**	DIBAL-H (2.1 equiv.)[b]	r.t.[b]	toluene	84[a]
5	**6e**	DIBAL-H (2.9 equiv.)	r.t.	–	86
6	**6f**	DIBAL-H (2.9 equiv.)	r.t.	–	0

[a] Conversion according to ^{31}P NMR of the reaction mixture. [b] DIBAL-H: diisobutylaluminium hydride; r.t.: room temperature.

Alane, prepared in situ from equimolar amounts of chlorotrimethylsilane and $LiAlH_4$ in diethyl ether (entry 2), was found to be less efficient. To move the reaction forward a continuous addition of new portions of alane was necessary.

Phosphinine **6e** was found to be inert towards $LiAlH_4$ but was successfully reduced with diisobutylaluminium hydride (DIBAL-H) in toluene at room temperature (entry 4). A solution of λ³-phosphinine **11** in toluene was distilled in vacuo into a low-temperature trap, and this distillate was used for further transformations.

To obtain pure λ³-phosphinine **11**, we conducted the reduction of **6e** under solvent-free conditions. As a result, we separated pure phosphinine **11** in 86 % yield. When we applied the same reduction conditions to phosphinine **6f**,[10a] a more sterically hindered analogue of phosphinine **6e**, the reaction did not run at all. Thus, we conclude that the reaction is very sensitive to steric factors. Studies of the possibility of applying this reaction to substituted phosphinines are underway in our laboratory, and the results will be reported in due course.

Conclusions

A set of novel parent λ⁵-phosphinines have been synthesized in high yields. The procedures can be run in a typical laboratory. A new method for the synthesis of parent λ³-phosphinine from available and inexpensive reagents starting from vinyl ethyl ether in five steps in a total yield of 30 % was developed. The current approach can probably be extended to other readily available λ⁵-phosphinines known in the literature.

Experimental Section

^{31}P NMR spectra were recorded with either a Gemini-200 (81 MHz) or Bruker Avance drx 500 (202 MHz) spectrometer with 85 % H_3PO_4 as an external standard. ^1H NMR spectra were recorded with Varian VXR-300 (300 MHz) or Bruker Avance drx 500 (500 MHz) spectrometers. ^{13}C NMR spectra were recorded with a Bruker Avance drx 500 (126 MHz) spectrometer. In ^1H and ^{13}C NMR spectra, chemical shifts are given with respect to deuterated solvents with residual peaks at δ = 7.26 and 77.2 ppm for $CDCl_3$, δ = 7.16 and 128.4 ppm for C_6D_6. Attached proton test (APT) experiments were used to assign signals in ^{13}C NMR spectra to different carbon atoms. All manipulations with chemicals were conducted under an atmosphere of argon by using Schlenk techniques. All experiments were repeated at least two times to ensure of their reproducibility.

λ³-Phosphinine (11)

Method A: A solution of dimethoxyphosphinine **6a** (0.59 g, 3.7 mmol) in diethyl ether (8 mL) was added dropwise to ice-cooled $LiAlH_4$ (0.15 g, 3.9 mmol). The resulting suspension was stirred at +35 °C for 68 h. The precipitate was separated by filtration (a filter with fine pores was used) and washed with diethyl ether. The ether was distilled off at atmospheric pressure, and the residue was distilled in vacuo (0.02 Torr) into a receiver cooled with liquid nitrogen. The product was obtained as a colorless liquid. Yield: 54 mg, 15 %.

Method B: To a stirred solution of *N*,*N*,*N*′,*N*′-tetramethyldiaminophosphinine **6e** (0.3 g, 1.6 mmol) in toluene (1.5 mL) cooled in an ice bath was added dropwise a toluene solution of DIBAL-H (2.1 mL, 3.4 mmol, 1.65 mol L^{-1}). The ice bath was removed, and the resulting solution was maintained at +16 °C for 24 h. A toluene solution of phosphabenzene was distilled in vacuo (0.02 Torr) into a receiver cooled with liquid nitrogen and used for further transformations.

Method C: *N*,*N*,*N*′,*N*′-Tetramethyldiaminophosphinine **6e** (2.0 g, 11 mmol) was added to cooled pure solid DIBAL-H (4.53 g, 32 mmol). The resulting mixture was warmed slowly to room temperature with stirring and maintained at room temperature overnight. Phosphabenzene was distilled in vacuo (0.02 Torr) into a receiver cooled with liquid nitrogen, affording the target compound as a colorless liquid. B.p. 93–94 °C (760 Torr). Yield: 0.90 g, 86 %.

^1H NMR (300 MHz, C_6D_6): δ = 7.09 (dt, J = 3.6, J = 8.1 Hz, 1 H, CH), 7.44 (qd, J = 8.2, J = 2.2 Hz, 2 H, CH), 8.50 (dd, $J_{P,H}$ = 37.5, $J_{H,H}$ = 10.2 Hz, 2 H, CH) ppm. $^{13}C\{^1H\}$ NMR (126 MHz, C_6D_6): δ = 129.5 (d, $J_{C,P}$ = 22.7 Hz, CH), 134.4 (d, $J_{C,P}$ = 15.1 Hz, CH), 155.0 (d, $J_{C,P}$ = 54.2 Hz, CH) ppm. ^{31}P NMR (202 MHz, C_6D_6): δ = 207.0 (tt, $^1J_{P,H}$ = 37.4, $J_{P,H}$ = 8.4 Hz) ppm.

CCDC-1055114 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Keywords: Phosphinines · Phosphahexatrienes · Electrochemistry · Cyclization · Reduction

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