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Selective Reductions in the Sphere of Organophosphorus Compounds

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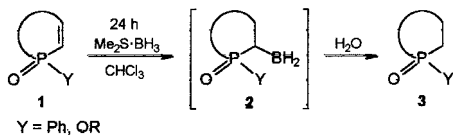
ABSTRACT: *Recent results on the selective reduction of cyclic vinylphosphine oxides and vinylphosphinates, as well as their refunctionalization by the use of borane, are summarized. The selective reduction of the phosphorus moiety of unsaturated phosphonates, phosphinates, and phosphine oxides is also discussed.* © 2001 John Wiley & Sons, Inc. Heteroatom Chem 12:161–167, 2001

INTRODUCTION

These days, the elaboration of selective syntheses is a great challenge for organic chemists. Many publications have appeared in the field of regioselectivity, stereoselectivity, and enantioselectivity. In this article, we briefly summarize our recent results on the subject of site-selective reductions of cyclic and acyclic phosphine oxides, phosphonates, and phosphinates.

Selective Reduction of the Double Bond of Cyclic Vinylphosphine Oxides/Vinylphosphinates

The reducing ability of borane can be well utilized in the saturation of the electron-poor double bond of cyclic vinyl phosphine oxides (**1**, Y = Ph) and phosphinates (**1**, Y = OR) (Scheme 1) [1–2]. The reduced product **3** is formed through hydroboration. Thus, the reaction of 2,3-dihydro-1H-phosphole oxides **4a,b** with the dimethyl sulfide borane (BMS) reagent gave the diastereomers of tetrahydrophosphole oxides **5a,b** in 53–97% yields (Table 1, entries 1 and 2). A similar reaction of dihydrophosphinine oxides **6** and **9** afforded tetrahydrophosphinine oxides **7** and **10**, respectively, in 48–65% yields (entries 3, 5, and 6). Due to the prochiral center in **4** and **6**, products **5** and **7** were obtained as a mixture of two diastereomers (entry 3). It is worthy of mention that the γ,δ-double bond of 1,2-dihydrophosphinine oxides **9a,b** remained intact (entries 5 and 6). By choice of appropriate reaction conditions, the reduction of 1,4-dihydrophosphinine oxide **6** could result in the reduction of both of the endocyclic unsaturations. It was, however, more suitable to use 1,2,3,4-tetrahydrophosphinine oxide **7** as the starting material in the synthesis of hexahydrophosphinine oxide **8** (entry 4). As exemplified in Scheme 2, the selective re-



SCHEME 1

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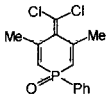
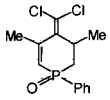
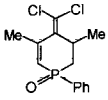
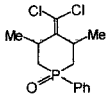
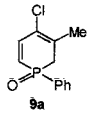
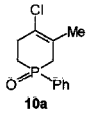
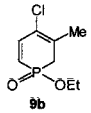
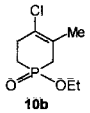
TABLE 1 Saturation of the Vinyl Moiety of Cyclic Phosphine Oxides and Phosphinates

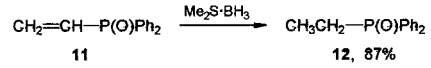
		Conditions				
Entry	*Starting Material*	*Quantity of BMS (equiv)*	*Temperature (°C)*	*Product*	*Yield (%) (isomeric comp. %)*	*Ref.*
(1)	 **4a**	2.2	26	 **5a**	97 (71–29)	[1]
(2)	 **4b**	2.2	63	 **5b**	53 (67–33)	[1]
(3)	 **6**	2.2	26	 **7**	51 (69–31)	[1]
(4)	 **7**	2.2	63	 **8**	44 (74–26)	[1]
(5)	 **9a**	1.05	24	 **10a**	65	[2]
(6)	 **9b**	1.05	40	 **10b**	48	[2]

duction could also be extended to alicyclic vinyl phosphine oxides [1].

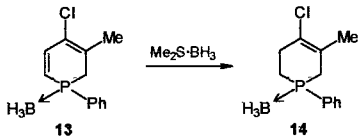
As a matter of fact, the selective saturation was first observed during the preparation of unsaturated phosphine boranes from the corresponding phosphines and BMS as described by Mathey [3], and later by us [4]. Thus, the synthesis of the dihydrophosphinine borane **13** was accompanied by the formation of tetrahydro derivative **14** (Scheme 3) [4]. Similarly, the preparation of phosphepine borane **15** was complicated by the formation of dihydrophosphepine **16** and tetrahydro derivative **17** (Scheme 4) [4].

Selective Reduction of the Phosphorus Moiety of Unsaturated Phosphonates and Phosphinates

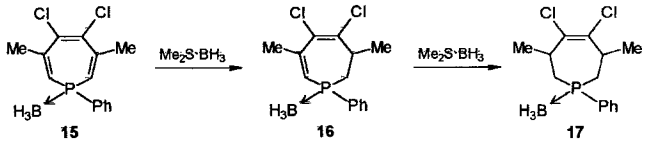
While the potential of the selective reductions discussed previously is that the P=O group remains intact, the reductions shown in this section take place in a contrary manner: the P=O moiety is deoxygen-



SCHEME 2 [Ref. 1]

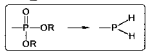


SCHEME 3 [Ref. 4]



SCHEME 4 [ref. 4]

ated, and the unsaturation remains unchanged. The use of alane derivatives ($AlHCl_2$) is an excellent choice to realize selective deoxygenations. $AlHCl_2$ can be prepared by a modification of the procedure described by Ashby [5], that is, by adding aluminum chloride into the tetraglyme solution of lithium aluminum hydride at −20°C. The application of alanes has an additional advantage: the alkoxy group(s) attached to the phosphorus moiety can also be reduced. Thus, the alane reduction of phosphinic esters leads to secondary phosphines, while the phosphonates are converted to primary phosphines. The low-boiling point free phosphines are directly distilled off under vacuum using tetraglyon as a solvent (see the apparatus, Figure 1). The nonvolatile phosphines are prepared in THF under atmospheric pressure. In the next two subsections, the application of these procedures to the synthesis of unsaturated phosphines is summarized.

The  *Transformation.* Primary vinylphosphines and ethynylphosphines are valuable intermediates, especially in the field of low-coordinated phosphorus species [6]. Before the spread of alanes, it was experienced that the reaction of diethyl vinylphosphonate (**18**) with lithium aluminiumhydride afforded nearly exclusively ethylphosphine (Scheme 5) [7]. The use of $AlHCl_2$ was an excellent choice to achieve the expected refunctionalization of diethyl vinylphosphonates **19**, obtained by the dehydrochlorination of α-chloro-ethylphosphonates prepared by the Arbuzov reaction (Scheme 6) [7]. The vinylphosphines **20**, obtained in 57–82% yields,

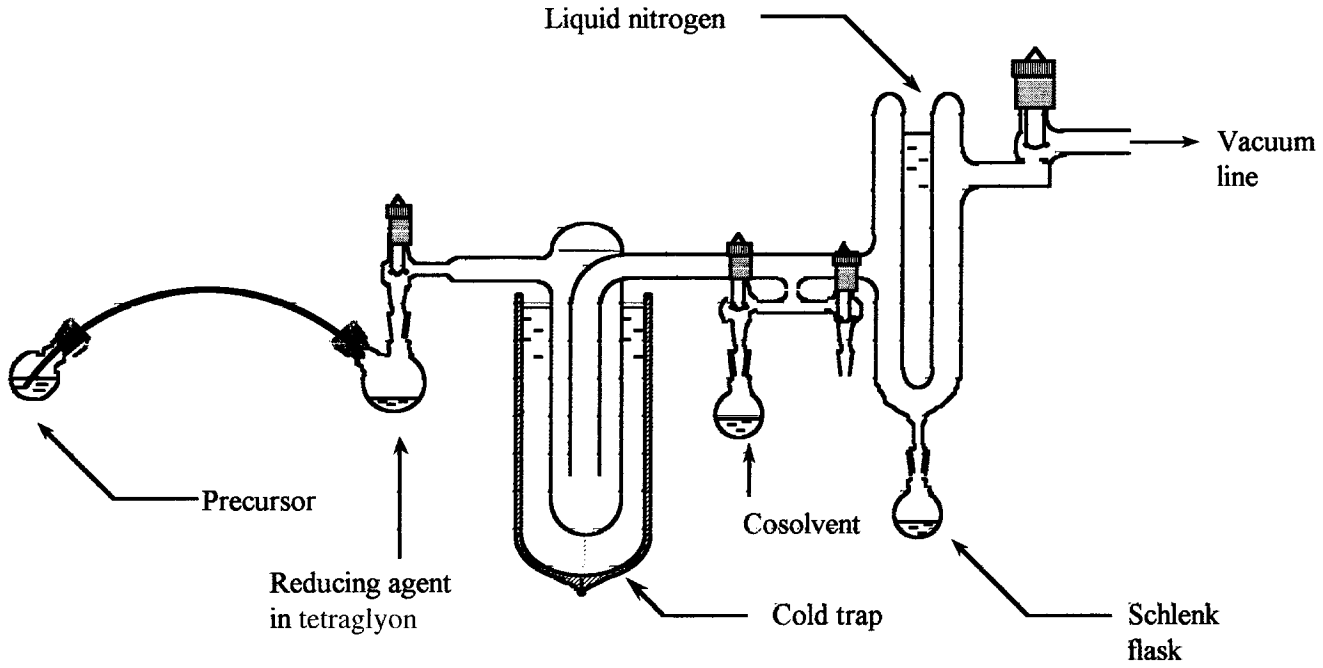
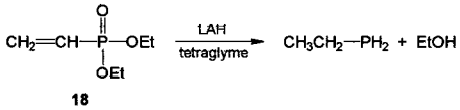


FIGURE 1



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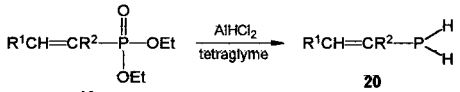
SCHEME 5 [Ref. 7]



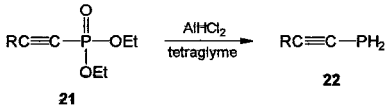
19 20

entry	R^1	R^2	yield [%]
(1)	H	H	76
(2)	H	Me	82
(3)	CH_2=CH–	H	63
(4)	Me	Cl	72
(5)	CH_2Cl–	H	57
(6)	CH_3CHCl–	H	72

SCHEME 6 [Ref. 8]

could be stored in a Schlenk tube at −10°C under nitrogen in the presence of a polymerization inhibitor.

The aforementioned method was also suitable for the reduction of diethyl ethynylphosphonates **21**. The low-boiling unsaturated phosphines (**22**) were obtained in 40% yield by vacuum trapping (Scheme 7) [8].

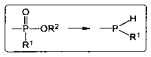


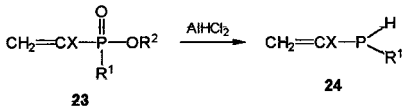
21 22

entry	R	yield [%]
(1)	H	40
(2)	Me	40
(3)	Me_3Si	40
(4)	Bu^n	40

SCHEME 7 [Ref. 8]

Another case of selectivity using alane was also reported by Japanese authors [9]. It has been observed recently by another group that phosphine oxides can be reduced chemoselectively to phosphines in excellent yields in the presence of other functional groups using alane [10].

The  *Transformation.* Secondary vinyl phosphine oxides are important starting compounds for low-coordinate species [6]. Scheme 8 shows the preparation of a variety of vinyl phosphines (**24**) by the chemoselective $AlHCl_2$ reduction of vinyl phosphinates (**23**) [11,12] that are easily available by the dehydrochlorination of α-chloroethylphosphinates prepared by the Arbuzov reaction. For reactions carried out at low temperature (−10°C) in mainly tetraglyme solvent, the phos-



23 **24**

entry	X	R^1	R^2	conditions: solvent	conditions: temperature [°C]	yield [%]	ref.
(1)	H	Me	Me	tetraglyme	–10	73	[11]
(2)	H	Bn	Et	tetraglyme	–10	82	[11]
(3)	H	allyl	Et	tetraglyme	–10	56	[11]
(4)	H	Ph	Et	tetraglyme	–10	20	[11]
(5)	Cl	Me	Et	THF	0	52	[12]

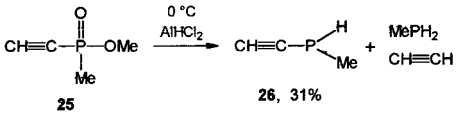
SCHEME 8

phines (**24**) were obtained in 20–82% yields after purification by trap-to-trap distillation (see the apparatus, Figure 1). In most cases, the formation of by-products resulting from C–P bond cleavage was negligible. This kind of side-reaction becomes predominant, however, in the alane reduction of ethynylphosphinate **25**. Phosphine **26** was obtained in only 31% yield due to the formation of methylphosphine and acetylene by-products (Scheme 9) [12]. The conventional method using phenylsilane [13] could be applied well to the deoxygenation of secondary ethynylphosphine oxides **27** to furnish the corresponding phosphines (**28**) in 55–75% yields (Scheme 10) [14]. In the last two instances, trichlorophenylsilane (a 33% ratio of $PhSiCl_3$ to $PhSiH_3$) was utilized (entries 6 and 7).

It can be seen that the silanes are suitable deoxygenating agents for phosphine oxides. It is well known, however, that the silane reduction of phosphinates and phosphonates leads to complex mixtures [13].

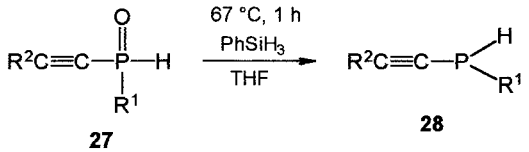
One-Pot Transformation of the Phosphine Oxide Function of P-Heterocycles to the Phosphine-Borane Moiety

We recall that the electron-poor double bond of vinylphosphine oxides can be reduced through hydroboration. It was also observed that the prolonged reaction of certain cyclic phosphine oxides (depicted by structure **29**) with a 3- to 4-fold excess of BMS under forcing conditions had resulted in a change of the P-function: the phosphine oxide group was transformed into a phosphine-borane function (Scheme 11) [15,16]. The only criterion for this new type of refunctionalization is that the starting cyclic phosphine oxide should have some ring strain. The decrease of the ring strain in pentacoordinate intermediate **31** is the driving force for the deoxygenation of phosphine oxide **29** that is the first step of the $P=O \rightarrow P \rightarrow BH_3$ refunctionalization (Scheme 11).



25 **26, 31%**

SCHEME 9 [Ref. 12]

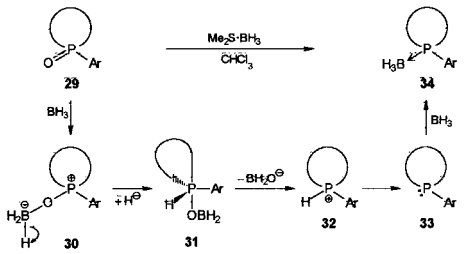


27 **28**

entry	R^1	R^2	yield [%]
(1)	Pr^i	H	65
(2)	Bu^t	H	55
(3)	Pr^i	Ph	70
(4)	Bu^t	Ph	70
(5)	Et	Ph	70
(6)	Ph	H	75*
(7)	Ph	Ph	75*

*$PhSiH_3$ / $PhSiCl_3$ (3 : 1), 30 °C, 15 min

SCHEME 10 [Ref. 14]

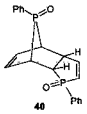
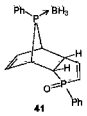
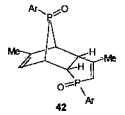
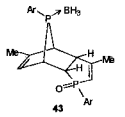
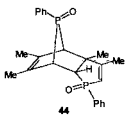
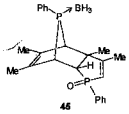


29 **30** **31** **32** **33** **34**

SCHEME 11

Three kinds of P-heterocycles having considerable ring strain were found to be especially suitable starting materials to undergo the above change: tetrahydrophospole oxides **5a** and **36**, 3-phosphabicyclo[3.1.0]hexane oxide **38**, and phosphole oxide dimers **40, 42**, and **44** (Table 2) [1,15,16]. The corresponding phosphine boranes (**35, 37, 39, 41, 43**, and **45**, respectively,) were obtained in 47–92% yields. Phosphine-boranes **37** and **39** were characterized by single crystal X-ray analysis [15]. The conversion of the tetrahydrophosphole oxides (**5a, 36**) and the phosphabicyclohexane oxides (**38**) to the boranes (**35, 37**, and **39**, respectively,) required three days of reflux in chloroform in the presence of 4.4 equivalents of BMS. At the same time, the modification of the phosphanorbornene 7-oxide moiety of dimers **40, 42**, and **44** required 21 hours of stirring at 26°C followed by a 7 hour reflux at 63°C using 3.0 equivalents of the BMS reagent (Table 2, entries 4–

TABLE 2 Refunctionalization of Cyclic Phosphine Oxides

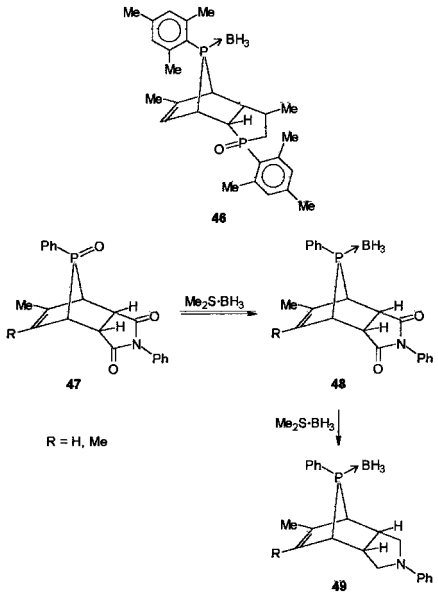
Entry	Starting Material	Conditions: Quantity of BMS (equiv.)	Conditions: Temperature (°C)	Reaction Time (h)	Product	Yield (%)	Ref.
(1)	 5a	4.5	63	72	 35	47	[1]
(2)	 36	4.4	63	72	 37	92	[15]
(3)	 38	4.4	63	72	 39	65	[15]
(4)	 40	3.0	1., 26 2., 63	21 7	 41	78	[16]
(5)	 42 Ar = Ph, 2,4,6-triMePh, 2,4,6-tri-PriPh	3.0	1., 26 2., 63	21 7	 43	74, 81, 68	[16]
(6)	 44	3.0	1., 26 2., 63	21 7	 45	72	[16]

6). The relatively mild conditions are in agreement with the extent of the ring strain of the phosphanorbornene framework; the C–P–C angle is 82° [17]. It is worthy of mention that the change in the P-function took place selectively, as the 2,3-dihydrophosphole moiety of the dimers (**40, 42**, and **44**) remained intact. Traces of the by-product (**46**) formed by selective reduction of the double bond in **43** (Ar = 2,4,6-triMePh) could, however, be detected in the crude reaction mixtures. Extension of the refunctionalization to other phosphanorbornene derivatives (**47**) was also possible. The reduction of the imide carbonyl groups of expected product **48** also took place resulting, however, in the formation of borane **49** (Scheme 12) [15].

The importance of the P=O → P → BH_3 transformation is that the conversion can be achieved in a one-pot synthesis. The phosphine-boranes are precursors of phosphines that can be used as ligands in some metal complexes as described in the review of Börner [18].

SUMMARY

The unsaturation of vinylphosphine oxides and vinyl phosphinates is selectively reduced by BMS. At the same time, the interaction of vinyl phosphonates and vinyl phosphinates with $AlHCl_2$ results in the reduction of the P-function, leaving the unsaturation intact. The P=O moiety of strained cyclic phosphine oxides is efficiently transformed to a P → BH_3 function by BMS.



SCHEME 12 [Ref. 15]

EXPERIMENTAL

General Procedure for the Reduction of the Unsaturation of Vinylphosphine Oxides

To the solution of vinylphosphine oxides (**4a,b, 6, 7, 9a,b**, and **11**) (2.0 mmol) in chloroform (15 mL) was added 1.05–2.2 equivalent of 2M borane-dimethyl sulfide in tetrahydrofuran (THF) (as shown in Table 1), and the mixture was stirred at 24–63°C (as shown in Table 1) for 24 hours. The mixture was hydrolyzed by stirring it with water (1 mL) for 5 minutes. The precipitated material was filtered off, and the organic phase was separated and dried ($MgSO_4$). The crude product obtained after evaporating the solvent was purified by column chromatography (silica gel, 3% MeOH in chloroform) to give products **5a,b, 7, 8, 10a,b**, and **12**, respectively as the mixture of two diastereomers. The purity of the phosphine oxides was 95–100%.

General Procedure for the Synthesis of Primary and Secondary Vinylphosphines by the Dichloroalane Reduction of Phosphonates and Phosphinates

Preparation of Dichloroalane ($AlHCl_2$). Dichloroalane ($AlHCl_2$) was prepared in THF or in tetraglyme. Both solvents were purified by refluxing over

and distillation from sodium/benzophenone under atmospheric pressure (THF) or under reduced pressure (tetraglyme). A 0.6 g (15.8 mmol) amount of lithium aluminum hydride in 80 mL of the solvent was cooled to −20°C, and 6.3 g (47.4 mmol) of aluminum trichloride was added during 20 minutes, in small portions, under a dry nitrogen atmosphere. The mixture was then stirred at room temperature for 30 minutes and used immediately in the following reductions.

Reduction of the Phosphonates and Phosphinates.

Caution: Free vinylphosphines are pyrophoric and cause nausea. All of the reactions must be carried out under dry nitrogen in a well-ventilated hood.

Procedure for the Preparation of Volatile Vinylphosphines (Method A). Volatile phosphines were prepared by the reduction of the corresponding phosphonates and phosphinates in tetraglyme under vacuum. The flask containing the reducing mixture, prepared as described previously, was attached to the vacuum line (Figure 1), and 24.3 mmol of the ester, previously cooled to −10°C, was slowly added to a two-necked flask with a flex needle through a septum. The flask was then allowed to warm to room temperature, and the vacuum was maintained for 2 hours. A cosolvent was added if it was necessary. During and after the addition of the ester, the evaporated tetraglyme was condensed on the cold trap maintained at −30°C, and the volatile phosphine was condensed on the liquid nitrogen cold trap. Subsequently, the liquid nitrogen was removed, and the product was collected in the Schlenck flask by vacuum transfer. The whole apparatus was then filled with dry nitrogen and the products, obtained in 55–90% yield, were characterized by ^{1}H, ^{13}C, and ^{31}P NMR and HR mass spectroscopy. The purity of the products was at least 95%. The main impurity was PH_3 or the corresponding primary phosphine resulting from the C–P cleavage.

Procedure for the Preparation of Nonvolatile Vinylphosphines (Method B). Nonvolatile vinylphosphines were prepared by the reduction of the corresponding phosphonates and phosphinates in THF under atmospheric pressure. The flask containing the reducing mixture, prepared as described previously, was cooled to −80°C, and the ester was slowly added to the flask through a dropping funnel. The mixture was vigorously stirred for 15 minutes and then allowed to warm to room temperature. The solution, transferred by use of a flex needle, was filtered through dried and degassed Celite under nitrogen pressure. To remove traces of hydrochloric acid, the solution obtained by filtration was transferred under nitrogen into a flask containing sodium hydrogencarbonate. This solution was suitable for further transformations. If it was necessary, purification could be performed by trap-to-trap distillation giving the phosphines in at least 50% yield. As in Method A, the main impurity was PH_3 or the corresponding primary phosphine resulting from the C–P cleavage.

Primary and secondary vinylphosphines were not too stable. They could, however, be kept for several weeks in a Schlenk flask at −10°C under nitrogen in the presence of a small amount of hydroquinone.

General Procedure for the Conversion of Cyclic Phosphine Oxides to Phosphine Boranes

To 1.12 mmol of the phosphine oxide (**5a, 36, 38, 40, 42**, and **44**) in 20 mL of absolute chloroform was added 3.0–4.5 equivalents of 2M dimethylsulfide borane in THF (as shown in Table 2), and the solution was stirred at 26–63°C for 28–72 hours (as shown in Table 2). After the addition of 2.0 mL of water, the mixture was stirred for 10 minutes and then filtered. The organic phase of the filtrate was separated and dried (Na_2SO_4). The crude product obtained after evaporating the volatile components was purified by column chromatography (silica gel, 2% methanol in chloroform) to give the products (**35, 37, 39, 41, 43**, and **45**) as crystalline or semicrystalline solids. The purity of the phosphine-boranes was 94–98%.

REFERENCES

[1] Keglevich, Gy.; Fekete, M.; Chuluunbaatar, T.; Dobó, A.; Böcskei, Zs.; Tőke, L. Synth Commun 2000, 30, 4221.
[2] (a) Keglevich, Gy.; Böcskei, Zs.; Újszászy, K.; Tőke, L. Synthesis 1997, 1391; (b) Keglevich, Gy.; Újszászy, K.; Ludányi, K.; Szöllősy, Á.; Tőke, L. Molecules 1997, 2, 46.
[3] Huy, H. T.; Mathey, F. Organometallics 1994, 13, 925.
[4] Keglevich, Gy.; Újszászy, K.; Szöllősy, Á.; Ludányi, K.; Tőke, L. J Organomet Chem 1996, 516, 139.
[5] Ashby, E. C.; Prather, J. J Am Chem Soc 1966, 88, 729.
[6] (a) Gaumont, A. C.; Denis, J. M. Chem Rev 1994, 94, 1413; (b) Gaumont, A. C.; Pellerin, B.; Cabioch, J. L.; Morise, X.; Lesvier, M.; Savignac, P.; Guenot, P.; Denis, J. M. Inorg Chem 1996, 35, 6667.
[7] Cabioch, J. L.; Denis, J. M. J Organomet Chem 1989, 377, 227.
[8] Guillemin, J. C.; Savignac, P.; Denis, J. M. Inorg Chem 1991, 30, 2171.
[9] Yamashita, M.; Ojima, I. J Am Chem Soc 1983, 105, 6339.
[10] Bootle-Wilbraham, A.; Head, S.; Longstaff, J.; Wyatt, P. Tetrahedron Lett 1999, 40, 5267.

[11] Gaumont, A. C.; Morrise, X.; Denis, J. M. J Org Chem 1992, 57, 4292.
[12] Guillemin, J. C.; Janati, T.; Denis, J. M.; Guenot, P.; Savignac, P. Tetrahedron Lett 1994, 35, 245.
[13] Engel, R. In Handbook of Organohosphorus Chemistry; Engel, R., Ed.; Marcel Dekker: New York, 1992, Chapter 5, p 200.
[14] Pilard, J. F.; Baba, G.; Gaumont, A. C.; Denis, J. M. Synlett 1995, 1168.
[15] Keglevich, Gy.; Fekete, M.; Chuluunbaatar, T.; Dobó, A.; Harmat, V.; Tőke, L. J Chem Soc Perkin Trans 1 2000, 4451.
[16] Keglevich, Gy.; Chuluunbaatar, T.; Ludányi, K.; Tőke, L. Tetrahedron 2000, 56, 1.
[17] Keglevich, Gy.; Böcskei, Zs.; Harmat, V.; Tőke, L. Heteroat Chem 1997, 8, 527.
[18] Börner, A. Synthesis 1998, 1391.