Synthesis of 1-Amino-2,5-dihydro-1*H*-phosphole 1-Oxides and Their *N*-Phosphinoyl Derivatives, Bis(2,5-dihydro-1*H*-phosphol-1-yl)amine *P*,*P*′-Dioxides

Nóra Zsuzsa Kiss,[a] András Simon,[b] László Drahos,[c] Krzysztof Huben,[d] Stefan Jankowski,[d] György Keglevich*[a]

[a] Department of Organic Chemistry and Technology, Budapest University of Technology and Economics, Műegyetem rkp.3, 1521 Budapest, Hungary

[b] Department of Inorganic and Analytical Chemistry, Budapest University of Technology and Economics, Műegyetem rkp.3, 1521 Budapest, Hungary

[c] Hungarian Academy of Sciences, Chemical Research Center, Pusztaszeri út 59-67, 1525 Budapest, Hungary

[d] Institute of Organic Chemistry, Faculty of Chemistry, Lodz University of Technology, Zeromskiego 116, 90-924 Łódź, Poland
Fax +36(1)4633648; E-mail: gkeglevich@mail.bme.hu

Received: 29.10.2012; Accepted after revision: 29.11.2012

Abstract: Depending on the molar ratio of the reactants and on the order of mixing, the reactions of a series of primary amines with 1-chloro-2,5-dihydro-1*H*-phosphole 1-oxides prepared in situ from the corresponding hydroxy-dihydrophosphole oxides afforded 1-amino-2,5-dihydro-1*H*-phosphole 1-oxides, or their *N*-phosphinoyl derivatives, bis(2,5-dihydro-1*H*-phosphol-1-yl)amine *P*,*P*′-dioxides. The latter family of P-heterocycles could also be synthesized by the reaction of 1-amino-2,5-dihydro-1*H*-phosphole oxides with chloro-dihydrophosphole oxides.

Key words: phosphorus, heterocycles, amides, phosphorylation, spectroscopy

The 2,5-dihydro- or 2,3-dihydro-1*H*-phosphole 1-oxides (2- and 3-phospholene 1-oxides), easily available by the McCormack cycloaddition and subsequent functionalization, form a representative group of P-heterocycles.[1–4] Quin and Mathey were the first chemists to explore systematically the field of phosphole derivatives.[1,3] Pietrusiewicz et al. elaborated novel methods for the modification of dihydrophosphole oxides based on C-alkylation, annulation, and epoxidation.[5–9] Yamashita synthesized 'phospha-sugars' on the basis of 2,3- and 3,4-dihydrophosphole oxides.[10–13] Keglevich et al. developed the ring opening of 2,5-dihydro-1*H*-phosphole oxides. Dichlorocarbene addition to the double bond of 2,5-dihydro-1*H*-phosphole oxides afforded 6,6-dichloro-3-phosphabicyclo[3.1.0]hexane 3-oxides that were converted into 1,2-dihydrophosphinine oxides by thermolysis.[14–16] 1,2-Dihydrophosphinine oxides are versatile intermediates in the preparation of more- and less-saturated phosphinine derivatives.[17,18] P-Heterocycles with a tervalent phosphorus atom may be novel ligands in transition-metal complexes.[19,20] These complexes may include optically active 2,5-dihydro-1*H*-phosphole ligands,[21] their precursors are the corresponding optically active 2,5-dihydro-1*H*-phosphole oxides obtained by resolution using methods developed by the senior author of this paper and co-workers.[22–24] The Michael reaction of 1-phenyl-2,3-dihydrophosphole oxide and diphenylphosphine oxide provides a 1-phosphinoyl-2,3,4,5-tetrahydro-1*H*-phosphole oxide[25] that is the precursor of LUPHOS.[26] Complexation of LUPHOS with platinum gave a *cis*-chelate complex.[27]

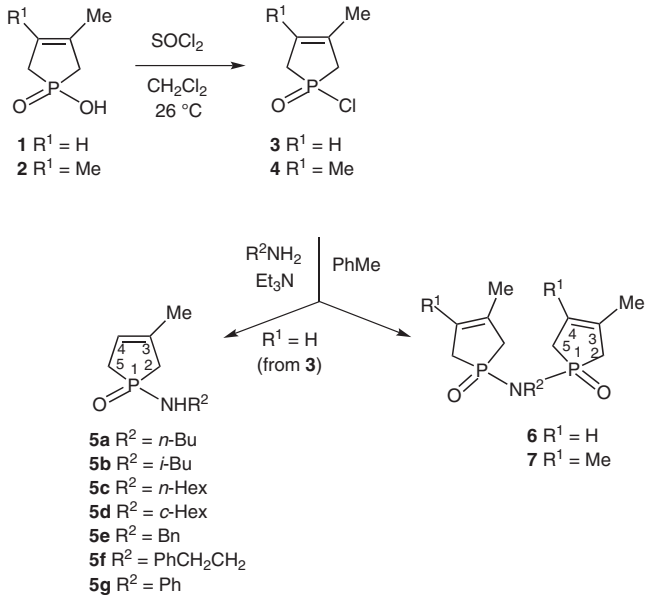
1-Amino-2,5-dihydrophosphole oxides are important intermediates.[28–30] On one hand, the trichlorosilane reduction of such species furnishes valuable 1-chloro-2,5-dihydro-1*H*-phospholes.[28] On the other hand, their reaction with dichlorocarbene results in the formation of versatile intermediates, 3-amino-3-phosphabicyclo[3.1.0]hexane 3-oxides.[29,30] A number of 1-amino-2,5-dihydrophosphole oxide derivatives[28,30–38] are known from the literature. The basic method for the preparation of these species involves the reaction of the corresponding halogeno-dihydrophosphole oxides, almost exclusively chlorides, with secondary amines,[31–33] or with primary amines.[30,34–37] In this paper, the synthesis of new N-monosubstituted 1-amino-2,5-dihydro-1*H*-phosphole 1-oxides and their *N*-phosphinoyl derivatives, bis(2,5-dihydro-1*H*-phosphol-1-yl)amine *P*,*P*′-dioxides is described. The latter series is a less studied family of compounds. Two analogous derivatives have been described, but no yields and spectral characterization was provided.[36]

In the first step of our syntheses, 1-hydroxy-2,5-dihydro-1*H*-phosphole 1-oxides **1** and **2** were converted into the corresponding 1-chloro derivatives **3** and **4** by reaction with thionyl chloride in dichloromethane at 26 °C for 24 hours.[29] Adding one equivalent of the primary amine, such as hexylamine, cyclohexylamine, or benzylamine, to the equimolar mixture of chloro-dihydrophosphole oxide **3** and triethylamine in toluene resulted in a mixture containing the expected 1-amino-2,5-dihydro-1*H*-phosphole oxides **5c**–**e** as minor products in 35–46% yields (with δ_P = 60.7–63.5). The major components, obtained in 54–65% yields, appeared at δ_P = 66.8–68.9 and proved to be bis(2,5-dihydro-1*H*-phosphol-1-yl)amine *P*,*P*′-dioxides **6c**–**e** after isolation and identification (Scheme 1). Next we tried to influence the product composition by adding the toluene solution of the chloro-dihydrophosphole oxide

SYNTHESIS 2013, 45, 0199–0204
Advanced online publication: 12.12.2012
DOI: 10.1055/s-0032-1316830; Art ID: SS-2012-T0862-OP

3 to an equimolar mixture of the corresponding primary amine and triethylamine. This had a dramatic impact on the product composition and the expected 1-amino-2,5-dihydro-1*H*-phosphole 1-oxides **5c**–**e** were formed as almost exclusive products (Scheme 1). This method was then applied to the synthesis of other amino-dihydrophosphole oxides **5a** and **5b** by the reaction of chloro-dihydrophosphole oxide **3** with butylamine and isobutylamine (Scheme 1).

The 1-amino-2,5-dihydro-1*H*-phosphole 1-oxides **5a**–**e** were obtained in 76–88% yields after purification by column chromatography and were characterized by ^{31}P, ^{13}C, and ^{1}H NMR, as well as mass spectral data.



Scheme 1

Then we returned to the original method, in which the amines, including also 2-phenylethylamine, aniline, and 4-methoxyaniline were added to a toluene solution of the 1-chloro-2,5-dihydro-1*H*-phosphole 1-oxide (**3**) and an equivalent of triethylamine, but the quantity of the amine was reduced to 0.5 equivalent. These experiments led to bis(2,5-dihydro-1*H*-phosphol-1-yl)amine *P*,*P*′-oxides **6a**–**g** as almost exclusive products (Scheme 1). The dimethyl derivatives **7a** and **7e** were synthesized in a similar way from chloro-dihydrophosphole oxide **4** (Scheme 1). The bis(2,5-dihydro-1*H*-phosphol-1-yl)amine *P*,*P*′-dioxides **6a**–**g** and **7a**,**e** were obtained in 72–95% yields after purification by chromatography. The structures of the products were supported by ^{31}P, ^{13}C, and ^{1}H NMR, as well as mass spectral parameters.

In the ^{13}C NMR spectra of bis(dihydrophospholyl)amine dioxides **7** comprising two 3,4-dimethyl-2,5-dihydro-1*H*-phosphol-1-yl moieties, the C_3 and the C_3–CH_3 carbon atoms appeared as a special multiplet, where the intensity of the middle peak was much lower than the other two peaks. The reason for this phenomenon is that, in these cases, the P_1, C_2, C_3, and C_3–CH_3 atoms of the two hetero rings are chemically equivalent, but magnetically not equivalent. Considering the natural abundance (1.1%) of the ^{13}C atoms, the multiplicity of these atoms may be described by the higher order spin system AA′X, where A is P, and X is C.[39] The multiplets were simplified to singlets on ^{31}P decoupling. The appearance of the signals for C_3 and C_3-CH_3 is shown in Figure 1, A. The multiplicity of the signals in the ^{13}C NMR spectra of bis(dihydrophospholyl)amine dioxides **6** including two 3-methyl-2,5-dihydro-1*H*-phosphol-1-yl units was similar, but the peaks were doubled as a consequence of the P-chiral centers. The ^{31}P decoupling again simplified the spectrum (Figure 1, B). For more information, the multiplicity of C_2 is also shown in Figure 1. The doublet became a singlet on ^{31}P decoupling. As a consequence of the P-chirality, products **6** were obtained as 1:1 mixtures of the *racemic* (*RR*/*SS*) and the *meso* (*RS*/*SR*) diastereomers. A good illustration of the isomeric composition of bis(dihydrophospholyl)amine dioxides **6** is shown by the pair lines for C_2 and C_3.

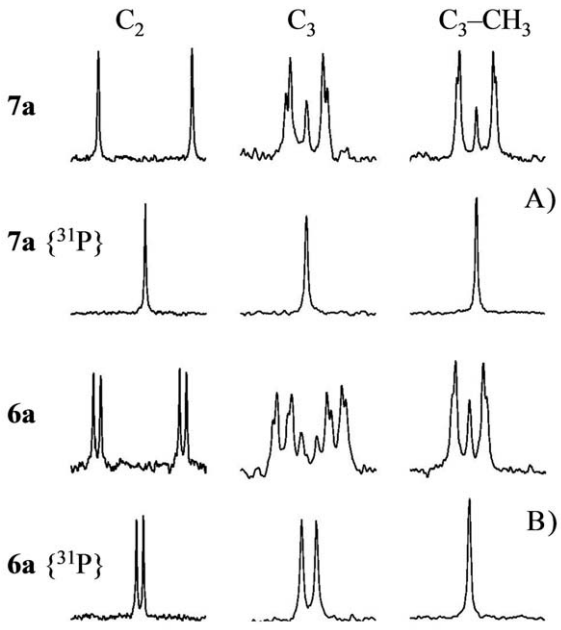
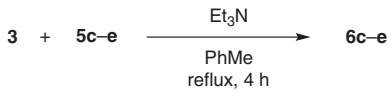


Figure 1 Segments from the ^{13}C NMR spectra of bis(2,5-dihydro-1*H*-phosphol-1-yl)amine *P*,*P*′-dioxides **6** and **7**

It seemed to be reasonable to try to prepare bis(dihydrophospholyl)amine dioxides **6c**–**e** by the reaction of 1-amino-2,5-dihydro-1*H*-phosphole 1-oxides **5c**–**e** with 1-chloro-2,5-dihydro-1*H*-phosphole 1-oxide **3**. In accord with expectation, the reactions were complete after reflux for four hours in toluene. The bis(dihydrophospholyl)amine dioxides **6c**–**e** were obtained in 58–83% yields after workup including flash chromatography (Scheme 2).



Scheme 2

^{31}P, ^{13}C, and ^{1}H NMR spectra were collected on a Bruker Avance-300 instrument operating at 121.5, 75.5, and 300 MHz, respectively. ^{31}P, ^{13}C, and ^{1}H NMR spectra of compounds **6a** and **7a** were obtained on a Bruker Avance-700 spectrometer at 283.4, 176, and 700 MHz, respectively, while ^{13}C {^{1}H,^{31}P} decoupled NMR spectra were recorded on a Bruker Avance-500 instrument at 125.8 MHz. The exact mass measurements were performed using a Q-TOF Premier mass spectrometer in positive electrospray mode.

1-Amino-3-methyl-2,5-dihydro-1*H*-phosphole 1-Oxide 5; General Procedure

To 1-hydroxy-3-methyl-2,5-dihydro-1*H*-phosphole 1-oxide (**1**, 1.5 g, 11.4 mmol) in anhyd CH_2Cl_2 (5 mL) was added $SOCl_2$ (1 mL, 13.8 mmol) and the mixture was stirred at 26 °C for 24 h. The solvent was evaporated and the volatile residues were removed under high vacuum. The 1-chloro-3-methyl-2,5-dihydro-1*H*-phosphole 1-oxide (**3**, 1.70 g, ~100%) so obtained was taken up in anhyd toluene (3 mL) and the resulting soln was added dropwise to a mixture of primary amine ($BuNH_2$: 1.14 mL, *i*-$BuNH_2$: 1.14 mL, $Me(CH_2)_5NH_2$: 1.5 mL, $CyNH_2$: 1.4 mL, $Ph(CH_2)_2NH_2$: 1.44 mL, $BnNH_2$: 1.3 mL, $PhNH_2$: 1.0 mL, 4-$MeOC_6H_4NH_2$: 1.32 mL; 11.4 mmol) and Et_3N (1.6 mL, 11.4 mmol) in toluene (3 mL) at 60 °C. The contents of the flask were stirred at reflux for 2 h. The amine hydrochloride salt was removed by filtration and the filtrate evaporated. The crude product was purified by column chromatography (silica gel, 3% MeOH–$CHCl_3$) to afford amino-dihydrophosphole oxide **5**.

1-(Butylamino)-3-methyl-2,5-dihydro-1*H*-phosphole 1-Oxide (5a)

Yellowish oil; yield: 1.8 g (85%).

IR (film): 2932, 1644, 1201, 1161, 770 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.91 (t, ^{3}J(HH) = 7.2 Hz, 3 H, CH_3CH$_2$), 1.28–1.42 (m, 2 H, CH_2), 1.44–1.58 (m, 2 H, CH_2), 1.79 (s, 3 H, C_3–CH_3), 2.12–2.60 (m, 5 H, 2 PCH_2, NH), 2.86–3.00 (m, 2 H, NCH_2), 5.51 (br d, ^{3}J(PH) = 33.0 Hz, 1 H, CH=).

^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 13.6 (*C*H_3CH$_2$), 19.8 (CH$_3$*C*H$_2$), 20.6 (^{3}J = 12.1 Hz, C_3–*C*H$_3$), 32.1 (^{1}J = 82.0 Hz, C_5), 34.1 (^{3}J = 6.2 Hz, NCH$_2$*C*H$_2$), 35.0 (^{1}J = 85.5 Hz, C_2), 40.3 (^{2}J = 1.8 Hz, NCH_2), 120.6 (^{2}J = 9.7 Hz, C_4), 136.6 (^{2}J = 15.2 Hz, C_3).

^{31}P NMR (121.5 MHz, $CDCl_3$): δ = 63.2.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_9H_{19}NOP$: 188.1204; found: 188.1210.

1-(Isobutylamino)-3-methyl-2,5-dihydro-1*H*-phosphole 1-Oxide (5b)

Yellowish oil; yield: 1.9 g (88%).

IR (film): 2931, 1643, 1200, 1164, 768 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.89 [d, ^{3}J(HH) = 6.7 Hz, 6 H, CH(CH_3)$_2$], 1.63–1.70 (m, 1 H, CH), 1.76 (s, 3 H, C_3–CH_3), 2.22–2.56 (m, 5 H, 2 PCH_2, NH), 2.67–2.74 (m, 2 H, NCH_2), 5.49 (br d, ^{3}J(PH) = 33.5 Hz, 1 H, CH=).

^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 19.8 [CH(*C*H$_3$)$_2$], 20.6 (^{3}J = 12.1 Hz, C_3–*C*H$_3$), 30.0 (^{3}J = 6.2 Hz, CH), 32.1 (^{1}J = 82.0 Hz, C_5), 34.9 (^{1}J = 85.5 Hz, C_2), 48.1 (^{2}J = 2.0, NCH_2), 120.6 (^{2}J = 9.7 Hz, C_4), 136.6 (^{2}J = 15.2 Hz, C_3).

^{31}P NMR (121.5 MHz, $CDCl_3$): δ = 63.6.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_9H_{19}NOP$: 188.1204; found: 188.1205.

1-(Hexylamino)-3-methyl-2,5-dihydro-1*H*-phosphole 1-Oxide (5c)

Yellowish oil; yield: 2.0 g (82%).

IR (film): 2930, 1643, 1200, 1166, 768 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.85 (t, ^{3}J(HH) = 6.2 Hz, 3 H, CH_3CH$_2$), 1.18–1.35 (m, 6 H, 3 CH_2), 1.41–1.55 (m, 2 H, CH_2), 1.76 (s, 3 H, C_3–CH_3), 2.18–2.57 (m, 5 H, 2 PCH_2, NH), 2.81–2.96 (m, 2 H, NCH_2), 5.48 (br d, ^{3}J(PH) = 33.4 Hz, 1 H, CH=).

^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 13.7 (*C*H_3CH$_2$), 20.4 (^{3}J = 12.1 Hz, C_3–*C*H$_3$), 22.3 (CH$_3$*C*H$_2$), 26.2 (CH_2), 31.2 (CH_2), 31.8 (^{3}J = 6.2 Hz, NCH$_2$*C*H$_2$), 31.9 (^{1}J = 82.0 Hz, C_5), 34.8 (^{1}J = 85.5 Hz, C_2), 40.4 (NCH_2), 120.5 (^{2}J = 9.6 Hz, C_4), 136.4 (^{2}J = 15.2 Hz, C_3).

^{31}P NMR (121.5 MHz, $CDCl_3$): δ = 63.1.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{11}H_{23}NOP$: 216.1517; found: 216.1527.

1-(Cyclohexylamino)-3-methyl-2,5-dihydro-1*H*-phosphole 1-Oxide (5d)

Yellowish oil; yield: 2.1 g (85%).

IR (film): 2931, 1646, 1200, 1165, 765 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.76 (s, C_3–CH_3) overlapped by 1.02–2.00 (m, 5 CH_2) (total 13 H), 2.15–2.60 (m, 5 H, NH, 2 PCH_2), 2.94–3.14 (m, 1 H, CH), 5.48 (br d, ^{3}J(PH) = 37.1 Hz, 1 H, CH=).

^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 20.5 (^{3}J = 12.1 Hz, C_3–*C*H$_3$), 24.9 ($C_{3'}$)*, 25.2 ($C_{4'}$), 33.1 (^{1}J = 82.2 Hz, C_5), 36.0 (^{1}J = 85.7 Hz, C_2), 36.1 (^{3}J = 4.0 Hz, $C_{2'}$)*, 49.9 ($C_{1'}$), 120.5 (^{2}J = 9.7 Hz, C_4), 136.4 (^{2}J = 15.2 Hz, C_3); * interchangeable.

^{31}P NMR (121.5 MHz, $CDCl_3$): δ = 60.7.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{11}H_{21}NOP$: 214.1361; found: 214.1369.

1-(Benzylamino)-3-methyl-2,5-dihydro-1*H*-phosphole 1-Oxide (5e)

Dense, yellowish oil; yield: 1.9 g (76%).

IR (film): 2935, 1640, 1206, 1160, 766 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.76 (s, 3 H, C_3–CH_3), 2.18–2.62 (m, 4 H, 2 PCH_2), 3.01–3.16 (m, 1 H, NH), 4.08–4.20 (m, 2 H, NHCH_2), 5.51 (br d, ^{3}J(PH) = 33.6 Hz, 1 H, CH=), 7.22–7.38 (m, 5 H, Ar).

^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 20.5 (^{3}J = 12.1 Hz, C_3–*C*H$_3$), 32.2 (^{1}J = 81.8 Hz, C_5), 35.0 (^{1}J = 85.3 Hz, C_2), 44.2 (NCH_2), 120.6 (^{2}J = 9.8 Hz, C_4), 127.3 ($C_{2'}$,* $C_{4'}$), 128.5 ($C_{3'}$)*, 136.6 (^{2}J = 15.3 Hz, C_3), 139.6 (^{3}J = 5.8 Hz, $C_{1'}$); * interchangeable.

^{31}P NMR (121.5 MHz, $CDCl_3$): δ = 63.5.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{12}H_{17}NOP$: 222.1048; found: 222.1051.

Bis(2,5-dihydro-1*H*-phosphol-1-yl)amine *P*,*P*′-Dioxides 6 and 7; General Procedure

To 1-hydroxy-3-methyl-2,5-dihydro-1*H*-phosphole 1-oxide (**1**, 0.5 g, 3.8 mmol) in anhyd CH_2Cl_2 (3 mL) was added $SOCl_2$ (0.35 mL, 4.7 mmol) and the mixture was stirred at 26 °C for 24 h. Then solvent was evaporated and the volatile components were removed under vacuum. The 1-chloro-3-methyl-2,5-dihydro-1*H*-phosphole 1-oxide (**3**, 0.57 g, ~100%) so obtained was taken up in anhyd toluene (5 mL) and Et_3N (0.53 mL, 3.8 mmol) was added. Then the primary amine ($BuNH_2$: 0.19 mL, *i*- $BuNH_2$: 0.19 mL, $Me(CH_2)_5NH_2$: 0.25 mL, $CyNH_2$: 0.22 mL, $Ph(CH_2)_2NH_2$: 0.24 mL, $BnNH_2$: 0.20 mL, $PhNH_2$: 0.17 mL, 4-$MeOC_6H_4NH_2$: 0.22 mL; 1.9 mmol) was added and the contents of the flask were stirred at reflux for 6 h. The amine hydrochloride salt was removed by filtration and the filtrate evaporated. The crude product so obtained was purified by column chromatography (silica gel, 3% MeOH–$CHCl_3$) to afford bis(2,5-

dihydro-1*H*-phosphol-1-yl)amine derivatives **6**. The dimethyl derivatives **7** were prepared in a similar way, starting from 1-hydroxy-3,4-dimethyl-2,5-dihydro-1*H*-phosphole 1-oxide (**2**, 0.55 g, 3.8 mmol) via intermediate 1-chloro-3,4-dimethyl-2,5-dihydro-1*H*-phosphole 1-oxide (**4**).

The following products were thus prepared:

Butylbis(3-methyl-2,5-dihydro-1*H*-phosphol-1-yl)amine *P*,*P*′-Dioxide (6a)
Slightly yellowish oil; yield: 0.54 g (95%).

IR (film): 2935, 1648, 1225, 1183, 781 cm^{-1}.

^1H NMR (700 MHz, $CDCl_3$): δ = 0.90 (t, ^3J(HH) = 7.4 Hz, 3 H, CH_3CH_2), 1.21–1.32 (m, 2 H, CH_2), 1.58–1.70 (m, 2 H, CH_2), 1.81 (s, 6 H, 2 C_3–CH_3), 2.41–2.79 (m, 8 H, 4 PCH_2), 3.04–3.15 (m, 2 H, NCH_2), 5.57 (br d, ^3J(PH) = 35.9 Hz, 2 H, 2 CH=).

^{13}C NMR (176 MHz, $CDCl_3$) {^1H}: δ = 13.9 (CH_3CH_2), 20.4 (CH_3CH_2), 20.8 (m, C_3–CH_3), 34.2 (NCH_2CH_2), 34.55 (d, ^1J = 80.0 Hz) and 34.61 (d, ^1J = 80.0 Hz) (C_5), 37.27 (d, ^1J = 83.6 Hz) and 37.32 (d, ^1J = 83.6 Hz) (C_2), 44.2 (NCH_2), 120.8 (m, C_4), 136.9 (m, C_3).

^{13}C NMR (125.8 MHz, $CDCl_3$) {^1H, ^{31}P}: δ = 13.9 (CH_3CH_2), 20.4 (CH_3CH_2), 20.8 (C_3–CH_3), 34.2 (NCH_2CH_2), 34.55 and 34.61 (C_2), 37.27 and 37.32 (C_5), 44.2 (NCH_2), 120.76 and 120.80 (C_4), 136.88 and 136.92 (C_3).

^{31}P NMR (283.4 MHz, $CDCl_3$): δ = 66.97 and 66.99.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{14}H_{26}NO_2P_2$: 302.1439; found: 302.1448.

Isobutylbis(3-methyl-2,5-dihydro-1*H*-phosphol-1-yl)amine *P*,*P*′-Dioxide (6b)
Slightly yellowish oil; yield: 0.30 g (53%).

IR (film): 2937, 1647, 1229, 1184, 779 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.93 [d, ^3J(HH) = 6.7 Hz, 6 H, $(CH_3)_2CH$], 1.81 (s, 6 H, 2 C_3–CH_3), 1.90–2.02 (m, 1 H, CH), 2.35–2.84 (m, 8 H, 4 PCH_2), 2.93–3.08 (m, 2 H, NCH_2), 5.57 (br d, ^3J(PH) = 36.0 Hz, 2 H, 2 CH=).

^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 19.7 [$CH(CH_3)_2$], 20.4 (m, ^3J = 13 Hz, C_3–CH_3), 29.1 (CH), 34.25 (^1J = 80.1 Hz) and 34.34 (^1J = 80.2 Hz) (C_5), 36.98 (^1J = 83.8 Hz) and 37.07 (^1J = 83.8 Hz) (C_2), 50.7 (NCH_2), 120.3 (m, ^2J = 11 Hz, C_4), 136.3 (m, ^2J = 16 Hz, C_3).

^{31}P NMR (121.5 MHz, $CDCl_3$): δ = 67.04 and 67.07.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{14}H_{26}NO_2P_2$: 302.1439; found: 302.1447.

Hexylbis(3-methyl-2,5-dihydro-1*H*-phosphol-1-yl)amine *P*,*P*′-Dioxide (6c)
Slightly yellowish oil; yield: 0.34 g (54%).

IR (film): 2930, 1646, 1233, 1184, 779 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.86 (t, ^3J(HH) = 6.6 Hz, 3 H, CH_3CH_2), 1.20–1.29 (m, 6 H, CH_2), 1.56–1.72 (m, 2 H, CH_2), 1.81 (s, 6 H, 2 C_3–CH_3), 2.36–2.81 (m, 8 H, 4 PCH_2), 2.98–3.18 (m, 2 H, NCH_2), 5.57 (br d, ^3J(PH) = 35.9 Hz, 2 H, 2 CH=).

^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 13.7 (CH_3CH_2), 20.4 (m, C_3–CH_3), 22.3 (CH_3CH_2), 26.4 (CH_2), 31.0 (CH_2), 31.6 (NCH_2CH_2), 34.16 (d, ^1J = 80.0 Hz) and 34.20 (d, ^1J = 80.0 Hz) (C_5), 36.87 (d, ^1J = 83.6 Hz) and 36.91 (d, ^1J = 83.6 Hz) (C_2), 44.0 (NCH_2), 120.4 (m, C_4), 136.5 (m, C_3).

^{31}P NMR (121.5 MHz, $CDCl_3$): δ = 66.67 and 66.68.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{16}H_{29}NO_2NaP_2$: 352.1571; found: 352.1573.

Cyclohexylbis(3-methyl-2,5-dihydro-1*H*-phosphol-1-yl)amine *P*,*P*′-Dioxide (6d)
Slightly yellowish oil; yield: 0.48 g (78%).

IR (film): 2932, 1648, 1231, 1182, 802 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.01–1.34 (m, 4 H, CH_2), 1.70–1.85, 1.81 (s, C_3–CH_3), overlapped by 1.70–1.85 (m, CH_2) (total 10 H), 2.30–2.88 (m, 11 H, 4 PCH_2, NCH, CH_2), 5.56 (br d, ^3J(PH) = 36.5 Hz, 2 H, 2 CH=).

^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 20.6 (m, C_3–CH_3), 24.8 ($C_{4''}$), 27.0 ($C_{3''}$), 33.1 (t, ^3J = 7.3 Hz, $C_{2''}$), 35.3 (d, ^1J = 78.5 Hz, C_5), 37.9 (d, ^1J = 78.5 Hz, C_2), 58.4 ($C_{1''}$), 120.6 (m, C_4), 136.7 (m, C_3).

^{31}P NMR (121.5 MHz, $CDCl_3$): δ = 64.6.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{28}NO_2P_2$: 328.1595; found: 328.1606.

Benzylbis(3-methyl-2,5-dihydro-1*H*-phosphol-1-yl)amine *P*,*P*′-Dioxide (6e)
Dense, slightly yellowish oil; yield: 0.60 g (95%).

IR (film): 2936, 1647, 1232, 1183, 779 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.76 (s, 6 H, 2 C_3–CH_3), 2.40–2.82 (m, 8 H, 4 PCH_2), 4.30–4.63 (m, 2 H, NCH_2), 5.55 (br d, ^3J(PH) = 36.3 Hz, 2 H, 2 CH=), 7.24–7.38 (m, 5 H, Ar).

^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 20.4 (m, ^3J = 13 Hz, C_3–CH_3), 33.94 (^1J = 79.5 Hz) and 33.97 (^1J = 79.4 Hz) (C_5), 36.66 (^1J = 83.1 Hz) and 36.70 (^1J = 83.1 Hz) (C_2), 46.18 (NCH_2), 120.43 and 120.50 (m, ^2J = 11 Hz, C_4), 126.5 ($C_{2''}$)*, 127.5 ($C_{4''}$), 128.6 ($C_{3''}$)*, 136.6 (m, ^2J = 17 Hz, C_3), 138.0 ($C_{1''}$); * interchangeable.

^{31}P NMR (121.5 MHz, $CDCl_3$): δ = 68.85 and 68.87.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{17}H_{24}NO_2P_2$: 336.1282; found: 336.1288.

Bis(3-methyl-2,5-dihydro-1*H*-phosphol-1-yl)(phenylethyl)amine *P*,*P*′-Dioxide (6f)
Slightly yellowish oil; yield: 0.61 g (93%).

IR (film): 2936, 1647, 1231, 1182, 763 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.81 (s, 6 H, 2 C_3–CH_3), 2.36–2.78 (m, 8 H, 4 PCH_2), 2.94–3.04 (m, 2 H, NCH_2CH_2), 3.18–3.42 (m, 2 H, NCH_2), 5.57 (br d, ^3J(PH) = 36.2 Hz, 2 H, 2 CH=), 7.13–7.34 (m, 5 H, Ar).

^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 20.3 (m, ^3J = 13 Hz, C_3–CH_3), 34.18 (^1J = 79.6 Hz) and 34.21 (^1J = 79.5 Hz) (C_5), 36.82 (^1J = 83.4 Hz) and 36.86 (^1J = 83.3 Hz) (C_2), 38.0 (NCH_2CH_2), 45.5 (NCH_2), 120.37 and 120.41 (m, ^2J = 11 Hz, C_4), 126.6 ($C_{4''}$), 128.5 ($C_{2''}$)*, 128.7 ($C_{3''}$)*, 136.45 and 136.49 (m, ^2J = 16 Hz, C_3), 138.0 ($C_{1''}$); * interchangeable.

^{31}P NMR (121.5 MHz, $CDCl_3$): δ = 67.6.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{18}H_{26}NO_2P_2$: 350.1439; found: 350.1447.

Bis(3-methyl-2,5-dihydro-1*H*-phosphol-1-yl)phenylamine *P*,*P*′-Dioxide (6g)
Slightly yellowish oil; yield: 0.44 g (72%).

IR (film): 2935, 1650, 1231, 1186, 774 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.66 (s, 6 H, 2 C_3–CH_3), 2.42–2.82 (m, 8 H, 4 PCH_2), 5.40 (br d, ^3J(PH) = 34.9 Hz, 2 H, 2 CH=), 7.29–7.44 (m, 5 H, Ar).

^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 20.2 (m, ^3J = 13 Hz, C_3–CH_3), 33. 4 (^1J = 82.2 Hz) (C_5), 36.1 (^1J = 85.9 Hz) (C_2), 120.3 (m, ^2J = 12 Hz, C_4), 128.3 (br s, $C_{4''}$), 128.8 (t, ^3J = 3.0 Hz, $C_{2''}$), 130.0 (br s, $C_{3''}$), 136.4 (m, ^2J = 18 Hz, C_3), 139.1 (br s, $C_{1''}$).

^{31}P NMR (121.5 MHz, $CDCl_3$): δ = 65.8.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{22}NO_2P_2$: 322.1126; found: 322.1130.

Butylbis(3,4-dimethyl-2,5-dihydro-1*H*-phosphol-1-yl)amine *P*,*P*′-Dioxide (7a)
Slightly yellowish oil; yield: 0.66 g (94%).

IR (film): 2932, 1611, 1235, 1186, 788 cm^{-1}.

^{1}H NMR (700 MHz, $CDCl_3$): δ = 0.89 (t, ^3J(HH) = 7.4 Hz, 3 H, CH_3CH_2), 1.19–1.34 (m, 2 H, CH_2), 1.55–1.66 (m, 2 H, CH_2), 1.72 (s, 12 H, 2 C_3–CH_3, 2 C_4–CH_3), 2.42–2.82 (m, 8 H, 4 PCH_2), 3.00–3.17 (m, 2 H, NCH_2).

^{13}C NMR (176 MHz, $CDCl_3$) {^{1}H}: δ = 13.8 (CH_3CH_2), 16.7 (m, C_3–CH_3), 20.4 (CH_3CH_2), 34.2 (NCH_2CH_2), 39.3 (d, ^1J = 82.5 Hz) (C_2), 44.4 (NCH_2), 128.0 (m, C_3).

^{13}C NMR (125.8 MHz, $CDCl_3$) {^{1}H, ^{31}P}: δ = 13.8 (CH_3CH_2), 16.7 (C_3–CH_3), 20.4 (CH_3CH_2), 34.2 (NCH_2CH_2), 39.3 (C_2), 44.4 (NCH_2), 128.0 (C_3).

^{31}P NMR (283.4 MHz, $CDCl_3$): δ = 59.7.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{30}NO_2P_2$: 330.1752; found: 330.1751.

Benzylbis(3,4-dimethyl-2,5-dihydro-1*H*-phosphol-1-yl)amine *P*,*P*′-Dioxide (7e)
Dense, slightly yellowish oil; yield: 0.62 g (90%).

IR (film): 2930, 1605, 1238, 1195, 763 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.68 (s, 12 H, 4 C_3–CH_3), 2.36–2.78 (m, 8 H, 4 PCH_2), 4.38–4.52 (m, 2 H, NCH_2), 7.23–7.38 (m, 5 H, Ar).

^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 16.4 (m, ^3J = 16 Hz, C_3–CH_3), 38.8 (^1J = 81.9 Hz) C_2, 46.5 (NCH_2), 126.5 ($C_{2''}$)*, 127.5 ($C_{4''}$), 127.8 (m, C_3), 128.7 ($C_{3''}$)*, 138.2 ($C_{1''}$); * interchangeable.

^{31}P NMR (121.5 MHz, $CDCl_3$): δ = 62.2.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{19}H_{28}NO_2P_2$: 364.1595; found: 364.1605.

Bis(3-methyl-2,5-dihydro-1*H*-phosphol-1-yl)amine *P*,*P*′-Oxides 6c–e by the Phosphinoylation of 1-Amino-3-methyl-2,5-dihydro-1*H*-phosphole 1-Oxides 5c–e; General Procedure
To 1-hydroxy-3-methyl-2,5-dihydro-1*H*-phosphole 1-oxide (**1**, 0.50 g, 3.8 mmol) in anhyd CH_2Cl_2 (3 mL) was added $SOCl_2$ (0.35 mL, 4.7 mmol) and the mixture was stirred at 26 °C for 24 h. The solvent was evaporated and the volatile components were removed under vacuum. The 1-chloro-3-methyl-2,5-dihydro-1*H*-phosphole 1-oxide (**3**, 0.57 g, ~100%) so obtained was taken up in anhyd toluene (3 mL) and Et_3N (0.53 mL, 3.79 mmol) was added. Then the soln of 1-amino-3-methyl-2,5-dihydro-1*H*-phosphole 1-oxides (**5c**: 0.82 g, **5d**: 0.82 g, **5e**: 0.84g; 3.8 mmol) in anhyd toluene (2 mL) was added. The contents of the flask were stirred at reflux for 4 h. Then the amine hydrochloride salt was removed by filtration and the filtrate evaporated. The crude product was purified by column chromatography (silica gel, 3% MeOH–$CHCl_3$) to afford bis(2,5-dihydro-1*H*-phospholyl)amine derivatives **6c**–**e**.

6c
Yield: 0.6 g (58%).

^{31}P NMR (121.5 MHz, $CDCl_3$): δ = 67.38 and 67.40.

6d
Yield: 1.0 g (83%).

^{31}P NMR (121.5 MHz, $CDCl_3$): δ = 66.9.

6e
Yield: 0.63 g (81%).

^{31}P NMR (121.5 MHz, $CDCl_3$): δ = 69.1.

Acknowledgment

This project was supported by the Hungarian Scientific and Research Fund (OTKA K83118).

References

(1) Quin, L. D. *The Heterocyclic Chemistry of Phosphorus: System Based on the Phosphorus–Carbon Bond*; Wiley: New York, **1981**, 30.
(2) Quin, L. D. In *Comprehensive Heterocyclic Chemistry II*; Vol. 2; Katritzky, A. R.; Rees, C. W.; Scriven, E. F. V., Eds.; Pergamon/Elsevier: Oxford, **1996**, Chap. 2.15, 826.
(3) *Phosphorus–Carbon Heterocyclic Chemistry: The Rise of a New Domain*; Mathey, F., Ed.; Pergamon: Amsterdam, **2001**, 195.
(4) Quin, L. D. *A Guide to Organophosphorus Chemistry*; Wiley & Sons: New York, **2000**, 249.
(5) Bodalski, R.; Pietrusiewicz, K. M.; Koszuk, J. *Tetrahedron* **1975**, *31*, 1907.
(6) Pakulski, Z.; Kwiatosz, R.; Pietrusiewicz, K. M. *Tetrahedron Lett.* **2003**, *44*, 5469.
(7) Pakulski, Z.; Kwiatosz, R.; Pietrusiewicz, K. M. *Tetrahedron* **2005**, *61*, 1481.
(8) Pakulski, Z.; Koprowski, M.; Pietrusiewicz, K. M. *Tetrahedron* **2003**, *59*, 8219.
(9) Pakulski, Z.; Pietrusiewicz, K. M. *Tetrahedron: Asymmetry* **2004**, *15*, 41.
(10) Haritha, B.; Reddy, V. K.; Oshikawa, T.; Yamashita, M. *Tetrahedron Lett.* **2004**, *45*, 1923.
(11) Yamada, M.; Yamashita, M.; Suyama, T.; Yamashita, J.; Asai, K.; Niimi, T.; Ozaki, N.; Fujie, M.; Maddali, K.; Nakamura, S.; Ohnishi, K. *Bioorg. Med. Chem. Lett.* **2010**, *20*, 5943.
(12) Reddy, V. K.; Haritha, B.; Oshikawa, T.; Yamashita, M. *Tetrahedron Lett.* **2004**, *45*, 2851.
(13) Yamashita, M.; Reddy, V. K.; Reddy, P. M.; Kato, Y.; Haritha, B.; Suzuki, K.; Takahashi, M.; Oshikawa, T. *Tetrahedron Lett.* **2003**, *44*, 3455.
(14) Keglevich, G. *Synthesis* **1993**, 931.
(15) Keglevich, G. *Rev. Heteroat. Chem.* **1996**, *14*, 119.
(16) Keglevich, G.; Tőke, L. *Trends Org. Chem.* **1993**, *4*, 245.
(17) Keglevich, G. *Curr. Org. Chem.* **2006**, *10*, 93.
(18) Keglevich, G. *Top. Heterocycl. Chem.* **2009**, *20*, 65.
(19) Kollár, L.; Keglevich, G. *Chem. Rev.* **2010**, *110*, 4257.
(20) Kerényi, A.; Kovács, V.; Körtvélyesi, T.; Ludányi, K.; Drahos, L.; Keglevich, G. *Heteroat. Chem.* **2010**, *21*, 63.
(21) Keglevich, G.; Bagi, P.; Szöllősy, Á.; Körtvélyesi, T.; Pongrácz, P.; Kollár, L.; Drahos, L. *J. Organomet. Chem.* **2011**, *696*, 3557.
(22) Novák, T.; Schindler, J.; Ujj, V.; Czugler, M.; Fogassy, E.; Keglevich, G. *Tetrahedron: Asymmetry* **2006**, *17*, 2599.
(23) Novák, T.; Ujj, V.; Schindler, J.; Czugler, M.; Kubinyi, M.; Mayer, Z. A.; Fogassy, E.; Keglevich, G. *Tetrahedron: Asymmetry* **2007**, *18*, 2965.
(24) Ujj, V.; Schindler, J.; Novák, T.; Czugler, M.; Fogassy, E.; Keglevich, G. *Tetrahedron: Asymmetry* **2008**, *19*, 1973.
(25) Jablonkai, E.; Drahos, L.; Drzazga, Z.; Koprowski, M.; Pietrusiewicz, K. M.; Keglevich, G. *Heteroat. Chem.* **2012**, DOI: 10.1002/hc.21047.
(26) Zablocka, M.; Boutonnet, F.; Igau, A.; Dahan, F.; Majoral, J. P.; Pietrusiewicz, K. M. *Angew. Chem. Int. Ed.* **1993**, *32*, 1735.
(27) Pietrusiewicz, K. M.; Flis, A.; Ujj, V.; Körtvélyesi, T.; Drahos, L.; Pongrácz, P.; Kollár, L.; Keglevich, G. *Heteroat. Chem.* **2011**, *22*, 730.

(28) Quin, L. D.; Szewczyk, J. *Phosphorus Sulfur Relat. Elem.* **1984**, *21*, 161.
(29) Keglevich, G.; Kovács, A.; Tőke, L.; Újszászy, K.; Argay, G.; Czugler, M.; Kálmán, A. *Heteroat. Chem.* **1993**, *4*, 329.
(30) Keglevich, G.; Dvorszki, J.; Ujj, V.; Ludányi, K. *Heteroat. Chem.* **2010**, *21*, 271.
(31) Quin, L. D.; Bourdieu, C.; Quin, G. S. *Phosphorus, Sulfur, Silicon Relat. Elem.* **1991**, *63*, 349.
(32) Arbuzov, B. A.; Vizel, A. O.; Zvelreva, M. A.; Studentsova, I. A.; Zaraev, R. S. *Russ. Chem. Bull.* **1966**, *15*, 1786.
(33) Maier, L.; Diel, P. J. *Phosphorus, Sulfur, Silicon Relat. Elem.* **1996**, *115*, 273.
(34) Szewczyk, J.; Lloyd, J. R.; Quin, L. D. *Phosphorus Sulfur Relat. Elem.* **1984**, *21*, 155.
(35) Weissman, S. A.; Baxter, S. G. *Tetrahedron Lett.* **1990**, *31*, 819.
(36) Kenn, M.; Jansen, W.; Schmitz-DuMont, O. *Z. Anorg. Allg. Chem.* **1979**, *452*, 176.
(37) Haritha, B.; Krishna Reddy, V.; Takahashi, M.; Yamashita, M. *Tetrahedron Lett.* **2004**, *45*, 5339.
(38) Hetherington, L.; Greedy, B.; Gouverneur, V. *Tetrahedron* **2000**, *56*, 2053.
(39) Quin, L. D.; Mesch, K. A.; Bodalski, R.; Pietrusiewicz, K. M. *Org. Magn. Res.* **1982**, *20*, 83.

