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New anellated 4*H*-1,4,2-diazaphospholes†

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Five new anellated 4*H*-1,4,2-diazaphospholes including the first examples of chiral 4*H*-1,4,2-diazaphospholes with the (−)-menthyl substituent have been prepared by two main routes: Hantzsch type cyclocondensation of 4-phenyl-2-amino-1,3-thiazole with chloromethyl dichlorophosphine and 4+1 cyclocondensation of cycloimmonium salts derived from 4-phenyl-2-amino-1,3-thiazole and 2-aminopyridine with PCl_3 and NEt_3. The new compounds have been characterized by multinuclear (^1H, ^{13}C, ^{31}P) NMR spectroscopy. Controlled hydrolysis of 5-phenylthiazolo[3,2-*d*][1,4,2]diazaphosphole **2a** with two equivalents of water yields the corresponding zwitterionic phosphinate **9**, the structure of which was elucidated by single crystal X-ray diffraction. The structure in the solid state is governed by strong N–H···O hydrogen bonding resulting in chains along the crystallographic *a*-axis. The chloroform molecules are integrated in the chains by weaker C–H···O bonds and C–Cl···C halogen bonds.

Introduction

Transition metal complexes of phosphines are widely used as catalysts in organic synthesis.[1,2] In particular chiral phosphines are of great interest as ligands, as they introduce chiral information in the catalyst and enable enantioselective cross coupling reactions,[3] hydrogenations[4] and hydroformylations.[5]

There is a series of prominent chiral phosphines used in asymmetric catalysis like (*R*)-BINAP,[6] ESPHOS[7] and TANIAPHOS[8] (Fig. 1). The synthesis of chiral phosphines and especially phosphines chiral at the phosphorus atom is in many cases quite laborious, however. Thus, there is still a need for a straightforward synthetic approach to chiral phosphines, which allows the variation of the substituents at phosphorus and in the organic backbone within a broad range.

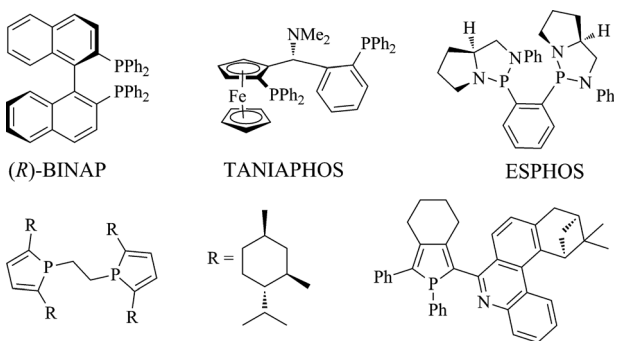

Fig. 1 Selected examples of chiral phosphines and phospholes.

Heterophospholes are a well established family of five-membered heterocycles with six delocalized π-electrons, which contain at least one two-coordinate tervalent phosphorus atom in the ring and in addition one heteroatom (N, O, S) contributing two π-electrons to the aromatic system. In the heterophospholes the dicoordinated phosphorus atom represents a prochiral center. Addition of reagents HX (X = OR′, NR'_2) to the P=C or P=N double bond in heterophospholes would generate a chiral center at the phosphorus atom and in the case of additions to the P=C bond possibly also at the adjacent carbon atom. Following this strategy heterocyclic chiral phosphines might become accessible, using heterophospholes as readily available starting materials.

Many heterophospholes and phospholes are described in the literature including some chiral phospholes (Fig. 1).[9] In contrast only a few chiral heterophosphole representatives have been reported (Fig. 2).[10,11]

In the course of our studies on the chemistry of heterophospholes[12a] we attempted the synthesis of chiral 1,4,2-diazaphospholes. The presence of chiral information in the

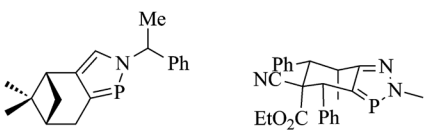

Fig. 2 Literature known chiral heterophospholes.

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† Electronic supplementary information (ESI) available: Additional bond lengths, bond angles and torsion angles of the crystal structure of compound **9**. CCDC 857096. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c2nj40709d

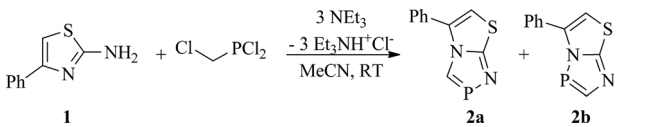
heterocycle might favour an enantioselective addition of HX to the P=C bond. Here we report on the synthesis of five new 4*H*-1,4,2-diazaphospholes (**2a**, **5a–c**, **6**) including two representatives with the chiral (−)-menthyl substituent (**5c**, **6**). The new compounds have been characterized by multinuclear (^{1}H, ^{13}C, ^{31}P) NMR spectroscopy. The reactivity of **2a** towards water has been investigated.

Results and discussion

Syntheses

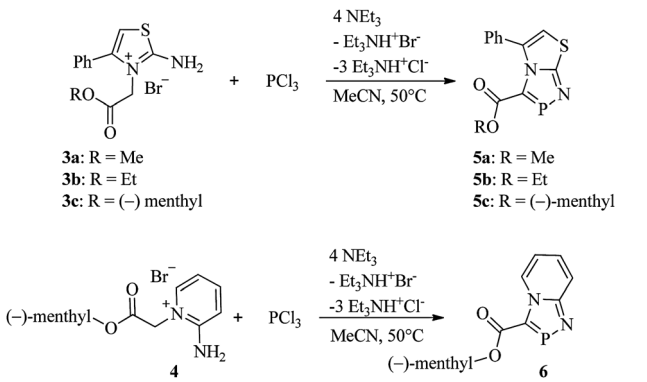
For the preparation of the new 4*H*-1,4,2-diazaphospholes synthetic protocols developed in our laboratory were used.[12,13] The Hantzsch-type 3+2 cyclocondensation of 2-amino-5-phenyl-1,3-thiazole (**1**) with chloromethyl dichlorophosphine in the presence of triethylamine yields the phenyl substituted diazaphosphole **2a** (Scheme 1). Of the two possible regioisomers **2a** and **2b** only one was formed. Its structure can be determined from the ^{1}H, ^{13}C and ^{31}P NMR spectra, which identify it unambiguously as the 4*H*-isomer **2a**. No signal corresponding to **2b** was observed in the ^{31}P NMR spectrum. This is in contrast to the analogous cyclocondensation with the unsubstituted 2-amino-1,3-thiazole, where a 7 : 1 mixture of the 1*H*- and 4*H*-regioisomers is formed with the 1*H*-isomer being the major product.[13]

The 4+1 cyclocondensation of the cycloimmonium salts **3a–c** and **4**[12e] with the equimolar amount of phosphorus trichloride and the fourfold amount of triethylamine yields the anellated 4*H*-1,4,2-diazaphospholes **5a–c** and **6**, respectively, as the only phosphorus containing products (Scheme 2). Starting from the (−)-menthyl esters **3c** and **4** the corresponding azaphospholes **5c** and **6** with the chiral (−)-menthyl substituent in the ester function were obtained. The reaction is slow and is completed in acetonitrile at 50 °C only after 7 days.



1 **2a** **2b**

Scheme 1 Synthesis of **2a** *via* a 3+2 cyclocondensation of **1** and chloromethyl dichlorophosphine.



Scheme 2 Synthesis of the 1,4,2-diazaphospoles **5a–c** and **6**.

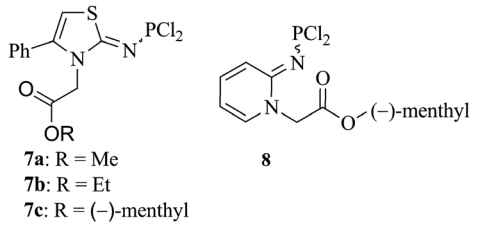


Fig. 3 Intermediate **7a–c** formed in the reaction yielding heterophospholes **5** and intermediate **8** leading to diazaphosphole **6**.

In the first step the aminodichlorophosphines **7a–c** and **8** are formed, as indicated by the ^{31}P NMR signal at 147.1 (**7a–c**) and 135.7 (**8**) (Fig. 3) observed after 24 h at ambient temperature.[14] The rate determining step seems to be the formation of the P–C bond.

Due to the similar solubility of the diazaphospholes and triethylammonium hydrochloride the separation of the products from the ammonium salt becomes difficult. The best protocol was found to be the extraction of the diazaphosphole with pentane or diethylether, which yielded only small amounts of the pure compound, however (see Experimental).

The new 4*H*-1,4,2-diazaphospholes were obtained as a colorless solid (**2a**) and white to yellow solids (**5a–c**, **6**). They are moisture sensitive and readily soluble in common organic solvents.

Their structure can be determined from the ^{1}H, ^{13}C and ^{31}P NMR spectra.

NMR spectra

The ^{31}P NMR and selected ^{13}C NMR data of **2a**, **5a–c** and **6** are summarized in Table 1. The ^{31}P NMR signals of the new 1,4,2-diazaphospholes are found at the low field (δ^{31}P = 215–255) in the same region as those of analogous anellated 4*H*-1,4,2-diazaphospoles.[12b,c,13] The ^{31}P NMR shifts of all compounds

Table 1 ^{31}P and selected ^{13}C NMR data of the 1,4,2-diazaphospholes **2**, **5a–c** and **6**, coupling constants *J* are given in Hz

	2a	5a	5b	5c	6
δ_P ($CDCl_3$)	223.6	251.6	251.4	252.1	229.8
δ_P (MeCN)	222.0	248.1	247.9	249.0	216.2
$^2J_{PH}$	32.0	—	—	—	—
δ_c ($CDCl_3$)					
C3	149.7	156.3	156.9	157.0	149.2
$^1J_{PC}$	66.2	68.7	69.0	70.4	69.5
C5	132.8	135.7	135.7	135.8	127.8
$^3J_{CP}$	[a]	2.2	2.0	2.0	[a]
C6	111.4	113.9	113.8	113.9	112.6
$^4J_{CP}$	0.6	1.5	1.4	1.3	2.5
C7/C7a	155.7	160.0	160.2	160.3	127.2
$^2J_{PC}$	17.9	17.7	17.8	17.6	—
C8	—	—	—	—	117.9
$^3J_{PC}$					9.5
C8a	—	—	—	—	153.2
$^2J_{PC}$					14.6
C=O	—	160.9	160.6	159.9	160.9
$^2J_{PC}$		15.7	15.5	14.8	13.9

[a] Not resolved.

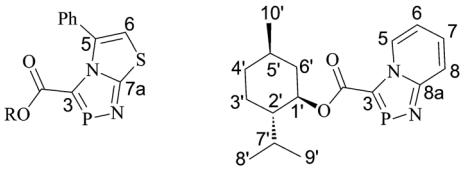


Fig. 4 Specific numbering used for the NMR data in Table 1.

show a remarkable dependency on the solvent used. The change from $CDCl_3$ to MeCN causes a high field shift of 1.6–13.6 ppm. This effect is small for the ^{31}P NMR signal of **2a** and large for **6**. In the case of **2a** a two bond P,H coupling of 32.0 Hz is observed, which is typical for the 4*H*-isomer.[13] The presence of a P–C bond results directly from the large P,C coupling constants, which range between 66 and 71 Hz and compare well to those found for other 4*H*-1,4,2-diazaphospholes. Values of $^2J_{PC}$ (around 17 Hz for **2a** and **5a–c**, and 14.6 Hz for **6**) are typical for P,C coupling over two bonds within the 1,4,2-diazaphosphole ring (Fig. 4).

Hydrolysis of 2a

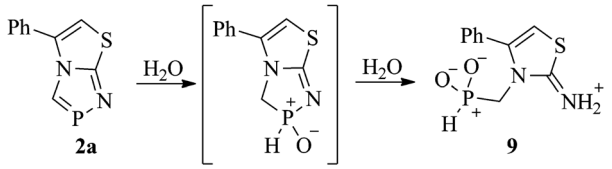
The diazaphospholes **2a**, **5a–c** and **6** are very sensitive towards moisture. Compound **2a** reacts readily with two equivalents of water in chloroform to give colorless crystalline aminophosphinic acid **9** with an aminothiazole ring in the organic backbone. Most probably in the initial step of the reaction the first equivalent of water adds to the P=C double bond to give an intermediate cyclic phosphine oxide. This intermediate reacts quickly with a second equivalent of water with a cleavage of the P–N bond to give the phosphinic acid **9** (Scheme 3).

Phosphinic acid displays a signal at $\delta_P = 11.7$ in the ^{31}P NMR spectrum with a large P,H coupling constant of 539.2 Hz. In the ^1H NMR spectrum a signal at the low field (10.56) corresponding to two NH protons is observed, which indicates a zwitterionic structure for **9** in solution. This zwitterionic structure is also confirmed for the solid state by the result of structure determination by single crystal X-ray diffraction.

Molecular and crystal structure of 9

Colourless block shaped single crystals of **9** suitable for X-ray diffraction were obtained by slow evaporation of a chloroform solution at ambient temperature. The compound crystallizes in the triclinic space group $P\bar{1}$ with two formula units in the unit cell. The asymmetric unit, depicted in Fig. 5, also contains one molecule of chloroform.

The result of the X-ray structure investigation reveals that the zwitterionic form **9** indicated by the ^1H NMR spectrum in



Scheme 3 Hydrolysis of compound **2a**.

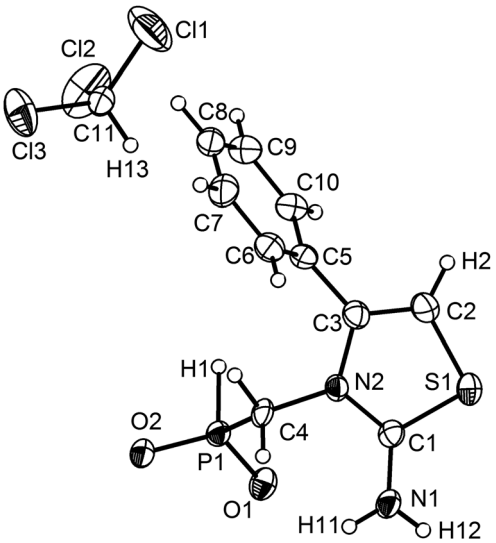


Fig. 5 ORTEP-drawing of the asymmetric unit of the crystal structure of compound **9** with atom labelling, including one solvent molecule ($CHCl_3$). Thermal ellipsoids are drawn at a 50% probability level.

solution is also present in the crystal. A closer look at the atom distances in the planar thiazaphosphole ring shows three different C–N distances: the distances C1–N1 (1.310(6) Å) and C1–N2 (1.348(5) Å) are shorter than the C–N single bond distance (1.47 Å)[15] and indicate a partial double bond character. On the other hand the C3–N2 distance of 1.416(5) Å corresponds to a C–N single bond. In accordance with this a short C2–C3 distance of 1.334(5) Å corresponding to a C=C double bond (1.33 Å)[15] is found. The phenyl ring is twisted out of the thiazole plane forming a N2–C3–C5–C6 dihedral angle of 59.0(5)°. All these data show practically no interaction among the π-systems of the phenyl ring, the C=C double bond and the N–C–N fragment in **9**. The atom distances in the molecule compare well to similar literature known structures.[16,17]

The crystal structure is governed by extensive hydrogen bonding involving the two protons of the NH_2 group and both oxygen atoms of the phosphinate moiety (Fig. 6, Table 2). Each molecule **9** is hydrogen bonded to two other molecules by four N–H···O bonds, acting two times as a H-donor *via* the NH_2 moiety and two times as a H-acceptor *via* both oxygen atoms of the phosphinate function. The N–H···O bonds are strong with H···O distances ranging between 1.93(3) and 1.96(3) Å (Table 2). These hydrogen bonds together with the shape of the molecule result in the formation of double chains arranged parallel to the crystallographic *a*-axis (Fig. 7). The double chains are completed by coordinated chloroform molecules, which are attached to O2 by a weaker C–H···O2 bond (2.11(4) Å) (Fig. 6). A similar coordination of chloroform to a P–O moiety with an O···H distance of 2.00(7) Å has been reported in the crystal structure of a bis(dicyclohexylphosphinito)platinum complex.[18] The coordination of the chloroform molecule to the double chain seems to be further favoured by the cooperative effect of the phenyl ring. Both, the phenyl ring and the chloroform molecule are rotated in such a way as to form a relatively strong

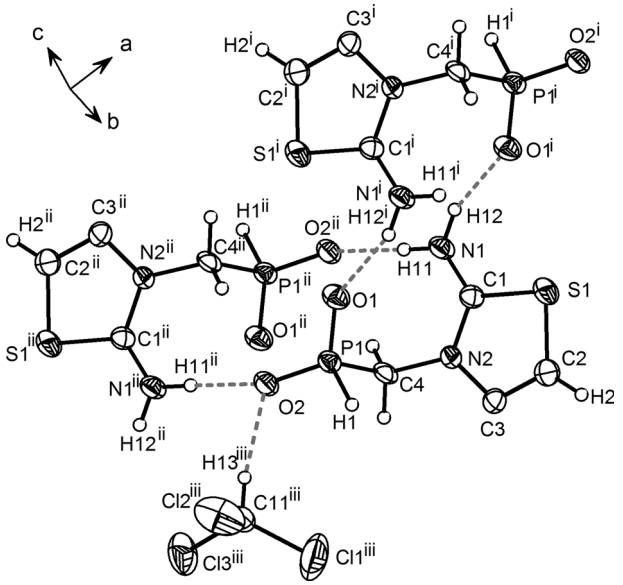


Fig. 6 ORTEP representation showing the hydrogen bonds in the crystal structure of **9**. The phenyl rings at C3 are omitted for clarity. Thermal ellipsoids are drawn at a 50% probability level. Symmetry codes: (i) (2 − *x*, −*y*, 1 − *z*); (ii) (1 − *x*, −*y*, 1 − *z*); (iii) (*x*, −1 + *y*, *z*).

Table 2 Structure parameters for the hydrogen bonds in the crystal structure of compound **9**. Distances in Å and angles in °. Symmetry codes: (i) (2 − *x*, −*y*, 1 − *z*); (ii) (1 − *x*, −*y*, 1 − *z*); (vi) (*x*, 1 + *y*, *z*)

X–Y···Z	*d* (X–Y)	*d* (Y···Z)	*d* (X–Z)	∢ (X–Y···Z)
N1–H11···O2^{ii}	0.88(3)	1.96(3)	2.822(5)	170(3)
N1–H12···O1^{ic}	0.86(3)	1.93(3)	2.734(4)	155(3)
C11–H13···O2^{vi}	0.92(4)	2.11(4)	3.023(5)	170(4)

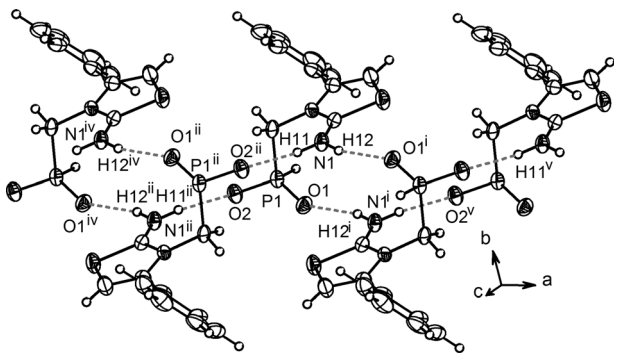


Fig. 7 Crystal structure of the zwitterionic phosphinate **9**. ORTEP representation of the hydrogen bonds (gray dashed lines) and the chains along the crystallographic *a*-axis. Solvent molecules are omitted for clarity. Thermal ellipsoids are drawn at a 50% probability level. Symmetry codes: (i) (2 − *x*, −*y*, 1 − *z*); (ii) (1 − *x*, −*y*, 1 − *z*); (iv) (−1 + *x*, *y*, *z*); (v) (1 + *x*, *y*, *z*).

halogen bond between Cl1 and the carbon atom at the *para* position C8 (3.261(5) Å). The corresponding bond angle C11–Cl1···C8 is 168.3(2)° (Fig. 8). Similar C···Cl distances between chloroform molecules and the *para* carbon atom of phenyl rings have been reported.[19]

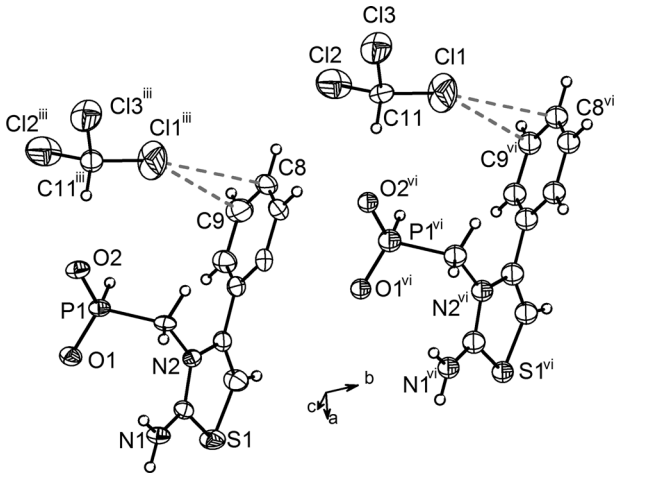


Fig. 8 ORTEP representation of the interaction between the halogen atom Cl1 of the chloroform molecule and the phenyl ring. Thermal ellipsoids are drawn at a 50% probability level. Symmetry codes: (iii) (*x*, −1 + *y*, *z*); (vi) (*x*, 1 + *y*, *z*).

Conclusions

The first examples of chiral anellated 4*H*-1,4,2-diazaphospholes have been prepared together with other new representatives. The synthetic route to chiral azaphospholes presented here opens the way to systematic investigations of 1,2-addition reactions to the P=C bond of these azaphospholes, which is anticipated to yield heterocyclic phosphines, chiral at the phosphorus atom. The controlled hydrolysis of anellated 4*H*-1,4,2-diazaphospholes, investigated using **2a** as an example, provides a synthetic route to phosphinates having heterocyclic moieties in the organic backbone. Such phosphinates are of interest due to possible biological activity. An interesting aspect of the structural chemistry of phosphinates derived from anellated 4*H*-1,4,2-diazaphospholes is the binding of halogen containing molecules *via* hydrogen and halogen bonding, as shown for the case of the thiazole derivative **9**.

Experimental section

General

All reactions were carried out under an inert gas atmosphere using Schlenk techniques. Argon (Messer Griesheim, purity 4.6 in a 50 L steel cylinder) was used as an inert gas. Glass vessels were stored in a 130 °C drying oven and were flame-dried in 10^{-3} mbar vacuum before use. The starting materials were prepared according to literature procedures.[12e,20] All other chemicals were commercially available and were used as received. The solvents were dried using commonly known drying methods and were freshly distilled before use.

NMR spectroscopy

NMR spectra were recorded using a JEOL EX 400 Eclipse instrument operating at 400.128 MHz (^{1}H), 100.626 MHz (^{13}C) and 161.835 MHz (^{31}P). Chemical shifts are referred to Me_4Si (^{1}H, ^{13}C) and 85% H_3PO_4 (^{31}P) as external standards. All spectra

were measured, if not mentioned otherwise, at 25 °C. Coupling constants are given in Hz.

Mass spectrometry

Mass spectrometric data were obtained using a JEOL Mstation JMS 700 spectrometer using the direct EI or DEI mode for neutral compounds and the FAB mode for ionic compounds with 4-nitrobenzyl alcohol as a matrix.

X-ray crystallography

The molecular structures in the crystalline state were determined using an Oxford Xcalibur3 diffraction instrument equipped with a Spellman generator (voltage 50 kV, current 40 mA) and a Kappa CCD detector, operating with Mo-Kα radiation (λ = 0.71073 Å). The data collection was performed with the CrysAlis CCD software[21] and the data reduction with the CrysAlis RED software.[22] The structure was solved with SIR-97,[23] refined with SHELXL-97[24] and finally checked using PLATON.[25] Absorption correction using the SCALE3 ABSPACK multiscan method[26] was applied.

All relevant data and parameters for the X-ray data collection and structure refinement are given in Table 3. Hydrogen atoms involved in hydrogen bonding were located in the difference Fourier map and refined isotropically. CCDC 857096.†

Syntheses

4-Phenyl-[1,4,2]diazaphospholo[5,4-*b*][1,3]thiazole (**2a**). In a 50 mL Schlenk flask equipped with a dropping funnel 2-amino-4-phenyl-1,3-thiazole (**1**) (1.76 g, 10 mmol, 1.0 eq.) was suspended in 20 mL of acetonitrile and cooled to 0 °C. At this temperature chloromethyl dichlorophosphine (1.0 mL, 10 mmol, 1.0 eq.) was added dropwise with stirring. Subsequently triethylamine (4.21 mL, 30 mmol, 3.0 eq.) dissolved in 5 mL of acetonitrile was added dropwise over a period of about 30 min. During this period triethylammonium chloride precipitated as a colorless solid and the solution turned yellow. The reaction mixture was allowed to reach room temperature and was stirred for 48 h. The reaction progress was monitored *via* ^{31}P NMR spectroscopy. After the reaction was complete all volatile compounds were removed *in vacuo* and the remaining solid was extracted with 20 mL of diethylether. The triethylammonium chloride was filtered off and after removing the solvent from the filtrate *in vacuo* 5-phenyl-[1,4,2]diazaphospholo[5,4-*b*][1,3]thiazole (**2a**) (0.39 g, 18%) was obtained as a colorless solid.

δ_P(162 MHz; $CDCl_3$; H_3PO_4) 223.6 (d, $^2J_{PH}$ = 32.0). δ_P(162 MHz; MeCN; H_3PO_4) 222.0 (s). δ_H(400 MHz; $CDCl_3$; Me_4Si) 7.01 (1H, d, $^5J_{PH}$ = 2.3, 6-H), 7.49–7.61 (5H, m, Ph), 9.06 (1H, d, $^2J_{PH}$ = 32.0, 3-H). δ_C(100 MHz; $CDCl_3$; Me_4Si) 111.4 (d, $^4J_{PC}$ = 0.6, C-6), 127.7 (C_o), 129.4 (C_m), 130.0 (C_p), 130.1 (C_i), 132.8 (C-5), 149.7 (d, $^1J_{PC}$ = 66.2, C-3), 155.7 (d, $^2J_{PC}$ = 17.9, C-7a). *m/z* 218.0 (M^+, 100%). HRMS (DEI+): M_{calc} = 218.0068, M_{found} = 218.0073 (100%).

Methyl-5-phenyl-[1,4,2]diazaphospholo[5,4-*b*][1,3]thiazole-3-carboxylate (**5a**). In a 50 mL Schlenk flask equipped with a dropping funnel 2-amino-3-(2-methoxy-2-oxoethyl)-4-phenyl-1,3-thiazol-3-ium bromide (**3a**) (0.33 g, 1 mmol, 1.0 eq.) was suspended in 10 mL of acetonitrile, trichlorophosphine (87.3 μL, 1 mmol, 1.0 eq.) was added and the mixture was cooled to 0 °C. A solution of triethylamine (0.55 mL, 4 mmol, 4.0 eq.) in 2 mL of acetonitrile was added dropwise over a period of about 15 min. During this period triethylammonium chloride precipitated as a colorless solid and the solution turned slightly yellow. The reaction mixture was allowed to reach room temperature and was stirred for seven days at 50 °C. The reaction progress was monitored *via* ^{31}P NMR spectroscopy. After the reaction was complete all volatile compounds were removed *in vacuo* and the remaining solid was extracted with 2 × 20 mL of diethylether–*n*-pentane mixture (3 : 1 v/v). After removing the solvent from the filtrates methyl 5-phenyl-[1,4,2]diazaphospholo[5,4-*b*][1,3]thiazole-3-carboxylate (**5a**) (41.70 mg, 15%) was obtained as a yellow solid.

δ_P(162 MHz; $CDCl_3$; H_3PO_4) 251.6 (s). δ_P(162 MHz; MeCN; H_3PO_4) 248.1 (s). δ_H(400 MHz; $CDCl_3$; Me_4Si) 3.39 (3H, s, OMe), 7.01 (1H, d, $^5J_{PH}$ = 2.4, 6-H), 7.36–7.45 (5H, m, Ph). δ_C(100 MHz; $CDCl_3$; Me_4Si) 51.9 (s, OMe), 113.9 (d, $^4J_{PC}$ = 1.5, C-6), 126.9 ($C_{m/o}$), 128.7 ($C_{m/o}$), 129.4 (C_p), 131.9 (d, $^4J_{PC}$ = 0.6, C_i), 135.7 (d, $^3J_{PC}$ = 2.2, C5), 156.3 (d, $^1J_{PC}$ = 68.7, C3), 160.0 (d, $^2J_{PC}$ = 17.7, C7a), 160.9 (d, $^2J_{PC}$ = 15.7, C=O). HRMS (DEI+): M_{calc} = 276.0122, M_{found} = 276.0128 (100%).

Ethyl-5-phenyl-[1,4,2]diazaphospholo[5,4-*b*][1,3]thiazole-3-carboxylate (**5b**). Compound **5b** was prepared following the same procedure as described for **5a** starting from 2-amino-3-(2-ethoxy-2-oxoethyl)-4-phenyl-1,3-thiazol-3-ium bromide (**3b**) (0.34 g, 1 mmol, 1.0 eq.), trichlorophosphine (87.3 μL, 1 mmol, 1.0 eq.) and triethylamine (0.55 mL, 4 mmol, 4.0 eq.). Ethyl-5-phenyl-[1,4,2]diazaphospholo[5,4-*b*][1,3]thiazole-3-carboxylate (**5b**) (22.9 mg, 8%) was obtained as a yellow solid.

Table 3 Crystal structure data of compound **9**

Formula	$C_{11}H_{12}Cl_3N_2O_2PS$
M	373.61
T, K	173(2)
Colour, habit	Colorless block
Cryst. size, mm	0.20 × 0.15 × 0.03
Crystal system	Triclinic
Space group	$P\bar{1}$ No.(2)
a, Å	7.5250(4)
b, Å	7.8787(6)
c, Å	14.2239(12)
α, °	99.852(7)
β, °	100.646(6)
γ, °	104.192(6)
V, Å^3	782.49(10)
Z	2
ρ_{calcd}, g cm^{-3}	1.586
μ, mm^{-1}	0.822
Irradiation, Å	0.71069
F(000)	380
Index ranges	$-8 \le h \le 8$ $-9 \le k \le 9$ $-16 \le l \le 16$
Reflns collected	9417
Reflns unique	2740
Reflns obsd	1875
R_{int}	0.0679
Params refined	194
θ range, °	4.31–25.00
R_1, wR_2 [$I > 2\sigma(I)$]	0.0563, 0.1120
R_1, wR_2 (all data)	0.0937, 0.1238
GooF	1.023
δp_{max}, δp_{min}/enm^{-3}	0.737, −0.611

δ_P(162 MHz; $CDCl_3$; H_3PO_4) 251.4 (s). δ_P(162 MHz; MeCN; H_3PO_4) 247.9 (s). δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.05 (3H, t, $^3J_{HH}$ = 7.1, OCH_2CH_3), 3.89 (2H, q, $^3J_{HH}$ = 7.1, OCH_2CH_3), 7.00 (1H, d, $^5J_{PH}$ = 2.4, 6-H), 7.36–7.46 (5H, m, Ph). δ_C(100 MHz; $CDCl_3$; Me_4Si) 14.0 (OCH_2CH_3), 61.3 (OCH_2CH_3), 113.8 (d, $^4J_{PC}$ = 1.4, C-6), 126.8 ($C_{m/o}$), 128.7 ($C_{m/o}$), 129.4 (C_p), 131.9 (C_i), 135.7 (d, $^3J_{PC}$ = 2.0, C-5), 156.9 (d, $^1J_{PC}$ = 69.0, C-3), 160.2 (d, $^2J_{PC}$ = 17.8, C-7$_a$), 160.6 (d, $^2J_{PC}$ = 15.5, *C*=O). HRMS (DEI+): M_{calc} = 290.0279, M_{found} = 290.0270 (83.4%).

(1*R*,2*S*,5*R*)-5-Methyl-2-(propan-2-yl)cyclohexyl-5-phenyl-[1,4,2]-diazaphospholo[5,4-*b*][1,3]thiazole-3-carboxylate (**5c**). Compound **5c** was prepared following the same procedure as described for **5a** starting from 2-amino-3-(2-((1*R*,2*S*,5*R*)-2-(propan-2-yl)-5-methylcyclohexyloxy)-2-oxoethyl)-4-phenyl-1,3-thiazol-3-ium bromide (**3c**) (0.45 g, 1 mmol, 1.0 eq.), trichlorophosphine (87.3 μL, 1 mmol, 1.0 eq.) and triethylamine (0.55 mL, 4 mmol, 4.0 eq.). Diazaphosphole (**5c**) (39.2 mg, 10%) was obtained as a yellow solid.

δ_P(162 MHz; $CDCl_3$; H_3PO_4) 252.1 (s). δ_P(162 MHz; MeCN; H_3PO_4) 249.0 (s). δ_H(400 MHz; $CDCl_3$; Me_4Si) 0.69 (3H, d, J = 7.0, 8′-Me), 0.76–0.83 (1H, m, 4′-H$_a$), 0.85 (3H, d, J = 6.5, 9′-Me), 0.90 (3H, d, J = 7.0, 10′-Me), 1.20–1.51 (2H, m, 3′-H$_a$, 6′-H$_a$), 1.51–1.67 (4H, m, 2′-H, 3′-H$_e$, 4′-H$_e$, 5′-H), 1.76–1.83 (1H, m, 7′-H), 1.91–1.99 (1H, m, 6′-H$_e$), 4.55 (1H, td, J = 10.9, 4.43, 1′-H), 7.00 (1H, d, $^5J_{PH}$ = 2.31, 6-H), 7.38–7.43 (5H, m, Ph). δ_C(100 MHz; $CDCl_3$; Me_4Si) 16.5 (C8′), 20.8 (C10′), 22.1 (C7′), 23.6 (C3′), 26.6 (C8′), 31.4 (C5′), 34.2 (C4′), 40.6 (C6′), 46.9 (C2′), 75.3 (C1′), 113.9 (d, $^4J_{PC}$ = 1.3, C6), 126.8 (C_o), 128.7 (C_m), 129.4 (C_p), 131.9 (C_i), 135.8 (d, $^3J_{PC}$ = 2.0, C5), 157.0 (d, $^1J_{PC}$ = 70.4, C3), 159.9 (d, $^2J_{PC}$ = 14.8, C=O), 160.3 (d, $^2J_{PC}$ = 17.6, C7$_a$). m/z 400.1 (M^+ 100%), 262.0 (100, M–menthyl$^+$). HRMS (DEI+): M_{calc} = 400.1374, M_{found} = 400.1364 (100%).

(1*R*,2*S*,5*R*)-5-Methyl-2-(propan-2-yl)cyclohexyl-[1,4,2]diazaphospholo[4,5-*a*]pyridine-3-carboxylate (**6**). Compound **6** was prepared following the same procedure as described for **5a** starting from 2-amino-1-(2-((1*R*,2*S*,5*R*)-2-(propan-2-yl)-5-methylcyclohexyloxy)-2-oxoethyl)pyridinium bromide (**4**) (0.37 g, 1 mmol, 1.0 eq.), trichlorophosphine (87.3 μL, 1 mmol, 1.0 eq.) and triethylamine (0.55 mL, 4 mmol, 4.0 eq.). Diazaphosphole (**6**) was obtained as a white solid (67.2 mg, 21%).

δ_P(162 MHz; $CDCl_3$; H_3PO_4) 229.9 (s). δ_P(162 MHz; MeCN; H_3PO_4) 216.2 (s). δ_H(400 MHz; $CDCl_3$; Me_4Si) 0.80 (3H, d, J = 7.0, 8′-Me), 0.89–0.93 (1H, m, 4′-H), 0.91 (3H, d, J = 7.0, 9′-Me), 0.93 (3H, d, J = 6.5, 10′-Me), 1.09–1.25 (2H, m, 3′-H$_a$, 6′-H$_a$), 1.49–1.64 (2H, m, 5′-H, 2′-H), 1.67–1.78 (2H, m, 3′-H$_e$, 4′-H$_e$), 1.92–2.04 (1H, m, 7′-H), 2.09–2.17 (1H, m, 6′-H$_e$), 5.00 (1H, td, J = 10.8, 4.4, 1′-H), 7.07–7.17 (1H, m, 5-H), 7.45–7.59 (1H, m, 8-H), 7.83–7.92 (1H, m, 7-H), 9.63–9.69 (1H, m, 6-H). δ_C(100 MHz; $CDCl_3$; Me_4Si) 15.1 (C8′), 19.1 (C10′), 20.4 (C7′), 22.2 (C3′), 25.1 (C9′), 29.9 (C5′), 32.6 (C4′), 39.4 (C6′), 45.5 (C2′), 73.4 (C1′), 112.6 (d, $^4J_{PC}$ = 2.5, C6), 117.9 (d, $^3J_{PC}$ = 9.5, C8), 127.2 (C7), 127.8 (C5), 149.2 (d, $^1J_{PC}$ = 69.5, C3), 153.2 (d, $^2J_{PC}$ = 14.6, C8a), 160.9 (d, $^2J_{PC}$ = 13.9, C=O). m/z 318.1 (M^+, 4%). HRMS (DEI+): M_{calc} = 318.1497, M_{found} = 318.1477 (69.7%).

(2-Imino-4-phenyl-1,3-thiazol-3-(2*H*)-yl)methyl phosphinate (**9**). In a 10 mL Schlenk flask compound **2a** (0.02 g, 0.92 mmol, 1.0 eq.) was dissolved in 5 mL of $CHCl_3$ and cooled to 0 °C. To this solution water (33.0 μL, 1.83 mmol, 2.0 eq.) was added *via* a microliter syringe while stirring. The clear solution became slightly turbid. The ^{31}P NMR spectrum showed the formation of the phosphinate **9**. Single crystals of **9**, suitable for X-ray diffraction, were obtained by slow evaporation of the chloroform solution at ambient temperature. For the NMR spectroscopic characterization the chloroform was evaporated *in vacuo* and the solid residue was dissolved in 0.6 mL of $CDCl_3$.

δ_P(162 MHz; $CDCl_3$; H_3PO_4) 11.7 (d, $^1J_{PH}$ = 539.2). δ_H(400 MHz; $CDCl_3$; Me_4Si) 4.13 (2H, d, $^2J_{PH}$ = 7.6, CH_2–P), 6.51 (1H, s, =C*H*–S), 7.07 (1H, d, $^1J_{PH}$ = 539.2, PH), 7.46–7.56 (5H, m, Ph), 10.56 (2H, br s, NH_2). δ_C(100 MHz; $CDCl_3$; Me_4Si) 49.1 (d, $^1J_{PC}$ = 82.0, CH_2–P), 104.5 (=*C*H–S), 128.7 (C_{Ar}), 129.2 (C_{Ar}), 130.1 (C_{Ar}), 130.4 (C_{Ar}), 141.5 (Ph–C–N), 170.1 (N–C=N). HRMS (DEI+): M_{calc} = 254.0279, M_{found} = 254.0289 (100%).

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