Novel Approaches to Fused Phospha-Pyrimidines

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Dedicated to Prof. A. Schmidpeter on the occasion of his 75th birthday

Abstract: Simple methods for the preparation of phosphorus-containing fused pyrimidine analogues such as fused 1,5,2-diazaphosphinines from amidine derivatives of π-excessive heterocycles are described. The scope and limitations of the methodology are detailed.

Key words: phospha-pyrimidines, amidines, phosphorus(III) halides, phosphorylation, heterocyclization

Recently Palacios and co-workers described a convenient approach to monocyclic 1,5,2-diazaphosphinines,[1] but there have been no general methods reported for the synthesis of fused phospha-pyrimidines.

Continuing our work on the synthesis of various phosphaheterocycles we decided to embark on the elaboration of a general approach to fused phospha-pyrimidines. Pyrazolo[3,4-*c*][1,5,2]diazaphosphinine systems **II** and **III** are the phospha-analogues of the pyrazolo[3,4-*d*]pyrimidine system **I**. They are also the phosphorous isostere of purine and possess a wide spectrum of biological activities, and therefore were chosen as our first target (Figure 1).[2,3]

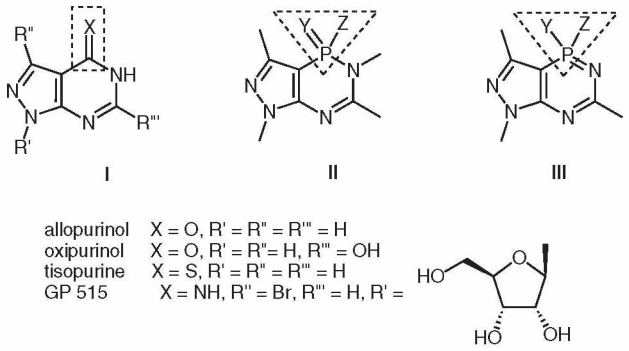
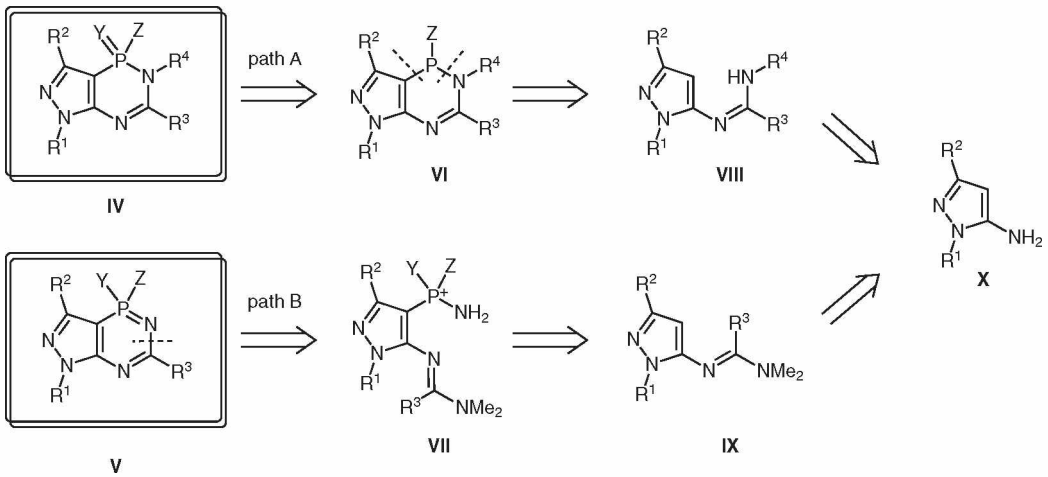


Figure 1

Direct phosphorylation of different substrates with phosphorus(III) halides can be used to form fused phosphaheterocycles. Schmidpeter and co-workers developed a method for the synthesis of two-coordinated phosphorus heterocycles,[4] which we used for the synthesis of various phosphaheterocycles incorporating a four-coordinated phosphorus atom.[5]



Scheme 1

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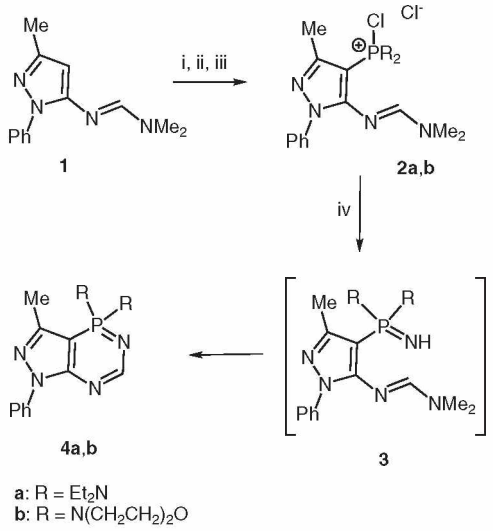
Two different pathways for the preparation of pyrazolo[3,4-*c*]diazaphosphinines **IV** and **V** based on the use of amidines **VIII** or **IX** is shown in Scheme 1. Path **A** involves the cyclocondensation of biselectrophilic phosphorus(III) halides with NH-amidine; a nucleophilic carbon atom on the pyrazole nucleus leading to the formation of two bonds, C–P and P–N, is the key step. In path **B** the key step is a 6-*exo*-*trig* cyclization of phosphonium salt **VII** with the formation of an N–C bond, giving a heterocycle.

Previously, we reported the synthesis of the 5*H*-1λ^5-pyrazolo[4,3-*c*][1,5,2]diazaphosphinine ring system starting from formamidine **1** (Scheme 2). Formamidine **1** was transformed into chlorophosphonium chloride **2** in three steps (one-pot). Then treatment of **2** with saturated ammonium solution in dichloromethane afforded iminophosphonate **3**, which spontaneously cyclized to diazaphosphinine **4**.[6]



Scheme 2 *Reagents and conditions*: (i) PCl_3, py, r.t., 1.5 h; (ii) amine, Et_3N, PhH, 1.5 h; (iii) C_2Cl_6, PhH; (iv) NH_3, CH_2Cl_2, 24 h.

We wished to extend this methodology to the synthesis of more complex 2,5-dihydro-1*H*-1λ^5-pyrazolo[4,3-*c*]-[1,5,2]diazaphosphinines **IV** (path **A**) by the reaction of amidines **VIII** with biselectrophilic phosphorus(III) halides and oxidation of the phosphorous(III) derivatives **VI**.[7]

We initially chose amidine **5** and looked at its reaction with phosphorous tribromide. The ^{1}H NMR spectrum of the reaction mixture revealed the intermediate formed by phosphorylation of the amidine exists as a pair of tautomers (Scheme 3). The phosphorotropic intermediates **6** and **7** are in equilibrium with each other but only the isomer **7** can undergo further heterocyclization to compound **8**. Indeed, heterocyclization in pyridine at room temperature was complete in ten minutes and afforded 5*H*-pyrazolo[4,3-*c*][1,5,2]diazaphosphinines, which are aza-analogues of pyrazolo[4,3-*c*][1,5,2]oxazaphosphinines (Scheme 3), which had been previously described by us.[5e]

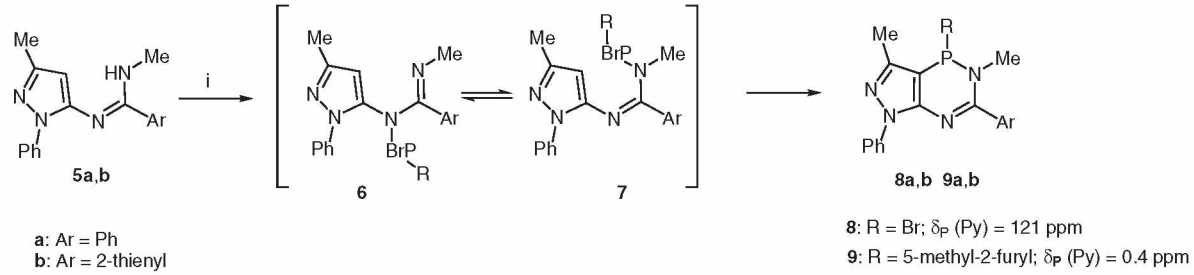
The ^{31}P NMR spectrum of the reaction mixture revealed only one signal at 121 ppm, which was assigned to the acid bromide **8**. Due to the high rate of reaction and its regioselectivity, the solution of acid bromide **8** in pyridine can be used without any additional purification. Acid bromide **8** is prone to undergo hydrolysis and reacts with moisture affording hydrophosphorylic compound **10**, but unlike 1-bromopyrazolo[4,3-*c*][1,5,2]oxazaphosphinines, with retention of the fused phospha-ring.[5e] Compound **10** in pyridine spontaneously undergoes oxidation in air giving cyclic phosphonic acid **11** (Scheme 4). Acid bromide **8** also reacts with amines and alcohols leading to amides **12** and esters **13**. It should be noted that an access of alcohol, similar to water, does not lead to the cleavage of the diazaphosphinine fused heterocyclic.[5e]

Phosphorus(III) derivatives **9**, **12**, and **13** can be oxidized to air-stable pentacoordinated phosphorus derivatives by various oxidants (Schemes 5– 7). Thus, the use of sulfur afforded a series of sulfides **14**, **18**, and **21**.

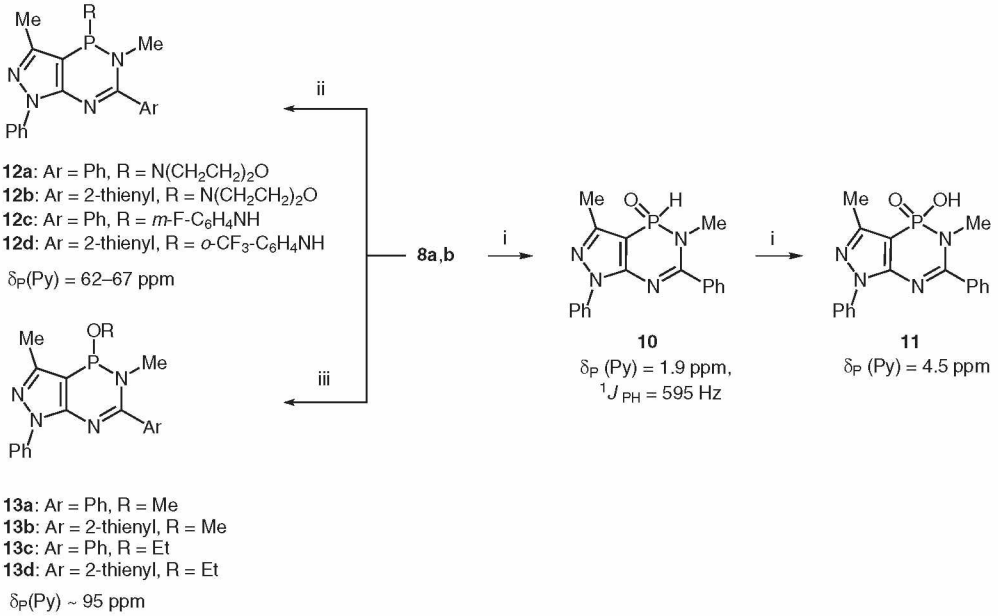
Amides **12** reacted readily with arylazides furnishing compounds **15**, that, unlike their pyrazolo[4,3-*c*][1,5,2]oxazaphosphinines analogues are hydrolytically stable.[5e] Treatment of esters **13** with arylazides afforded the corresponding imino compounds, which underwent hydrolysis to amides **20**.

Pentavalent amides **17** were prepared by hydrolysis of bromophosphonium salt **16** which, in turn, was synthesized from the reaction of amides **12** with bromine.

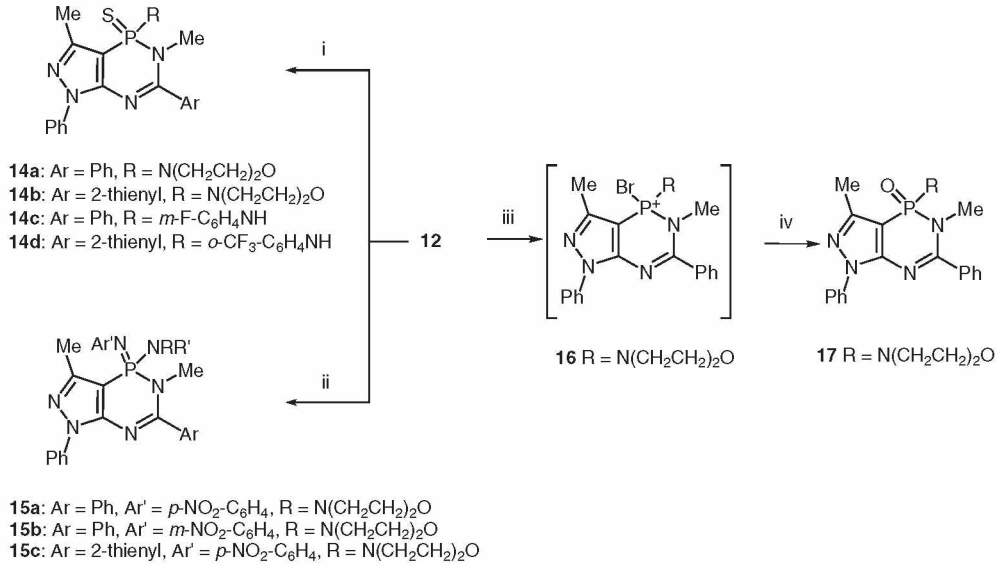
The structures of compounds **11**, **14**, **15**, **17**, **20**, and **21** were confirmed by ^{1}H, ^{13}C, and ^{31}P NMR spectroscopy, mass spectrometry, and elemental analysis. The ^{1}H NMR spectra revealed the absence of the 4H-pyrazole proton (ca. 4.90 ppm, s) and the amidine proton (ca. 7.85, br q, $^3J_{HH}$ = 4.5 Hz), thus confirming the presence of the fused phospha-cycle. The coupling constant of the NMe group



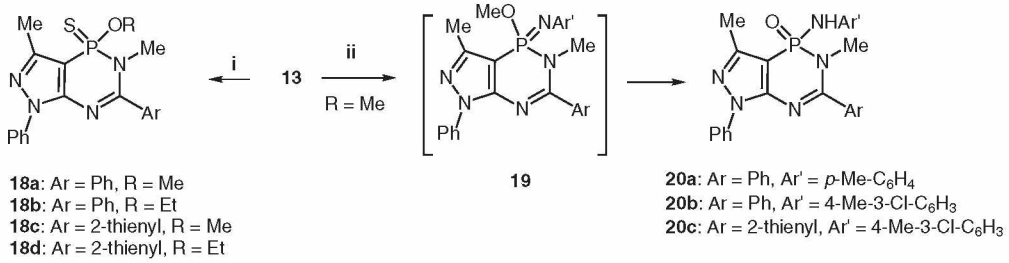
Scheme 3 *Reagents and conditions*: (i) for **8**: PBr_3, py, r.t., 10 min; for **9**: 5-methyl-5-furyl-PBr_2, Py, r.t., 1 h.



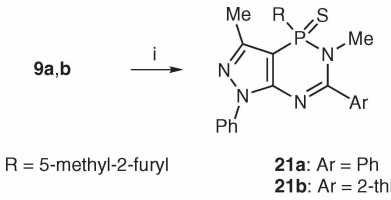
Scheme 4 *Reagents and conditions:* (i) air, py, r.t., 12 h; (ii) amine, py, r.t., 5 min; (iii) ROH, py, r.t., 10 min.



Scheme 5 *Reagents and conditions*: (i) S, py, r.t., 1 h; (ii) ArN_3, py, 50 °C, 1 h; (iii) Br_2, PhH, r.t., 10 min; (iv) aq $NaHCO_3$



Scheme 6 *Reagents and conditions:* (i) S, py, r.t., 12 h; (ii) ArN_3, py, r.t., 5 min; (iii) ROH, py, r.t., 10 min

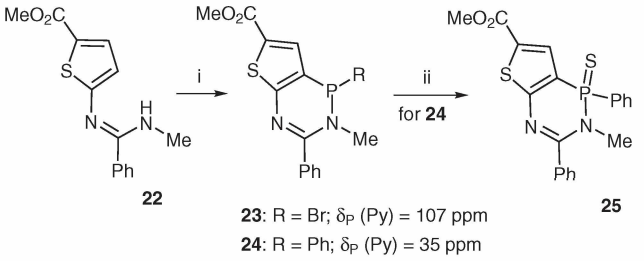


Scheme 7 *Reagents and conditions:* (i) S, py, r.t., 1 h.

had increased by around 3 ppm ($^3J_{HH}$ ca. 4 Hz to $^3J_{HP}$ ca. 7–9 Hz), which along with the presence of C7a in the ^{13}C NMR spectra (**17**: 92.3 ppm $^1J_{CP}$ = 186.5 Hz) also confirmed the presence of the cyclic pentaphosphine derivatives.

Our approach to the pyrazolo[3,4-*c*]diazaphosphinine ring system can be extended to derivatives of other aminoheterocycles. Previously 2-aminothiophene and 2-aminofuran have been shown to undergo similar reactions to 5-aminopyrazoles.[8,9]

Similar to aminopyrazole derivatives **5**, amidine **22**, a derivative of aminothiophene, undergoes heterocyclization with PBr_3 and $PhPBr_2$ resulting in 1,2-dihydrothieno[3,2-*c*][1,5,2]diazaphosphinine ring systems **23** and **24**, respectively (Scheme 8). The reaction is rapid and regioselective so that it is possible to use **23** and **24** in situ for further transformations. Phosphine **24** was oxidized with sulfur into stable phosphine sulfide **25**.

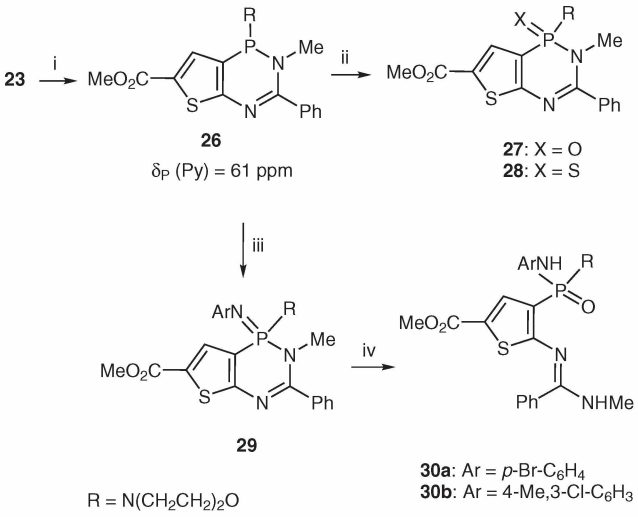


Scheme 8 *Reagents and conditions:* (i) for **23**: PBr_3, py, r.t., 3 h; for **24**: $PhPBr_2$, py, r.t., 3 h; (ii) S, py, r.t., 1 h.

Cyclic acid bromide **23** was also used for the preparation of various stable pentavalent derivatives. Unfortunately, unlike acid bromide **8**, compound **23** only reacts selectively with amines, while reactions with O-nucleophiles such as water and alcohols is not selective and has no preparative value. Thus, amide **26** was transformed into cyclic phosphine oxide and sulfide **27** and **28**, respectively.

The amide **26** also reacts well with arylazides affording iminophosphonates **29**, which, contrary to analogous derivatives **15**, are hydrolytically unstable and in the presence of water undergo cleavage of the heterocycle leading to acyclic amidine derivatives **30** (Scheme 9).

Typical features in the ^1H NMR spectrum which reveal the presence of the fused heterocyclic ring are the disappearance of the signals corresponding to the 3-H of thiophene (**22**: 6.06 ppm, d, $^3J_{HH}$ = 3.9 Hz) and the amidine proton (**22**: 7.88, br q, $^3J_{HH}$ = 4.5 Hz). The coupling



Scheme 9 *Reagents and conditions:* (i) amine, py, r.t., 5 min; (ii) for **27**: H_2O_2, benzene, r.t.; for **28**: S, py, r.t., 1 h, (iii) ArN_3, py, 50 °C, 1 h; (iv) H_2O, py.

constant representing the doublet corresponding to the NMe group increased upon cyclization (from $^3J_{HH}$ ca. 4 Hz to $^3J_{HP}$ ca. 7–9 Hz). Additional proof that the C–P bond was present was found in the ^{13}C NMR spectra, a doublet corresponding to C7a appeared (**27**: 111.2, $^1J_{CP}$ = 196 Hz). Finally, the structure of **27** was solved by X-ray diffraction (Figure 2).

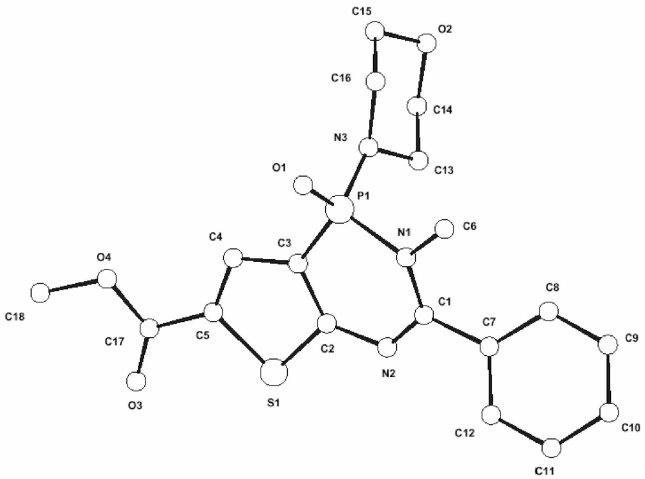
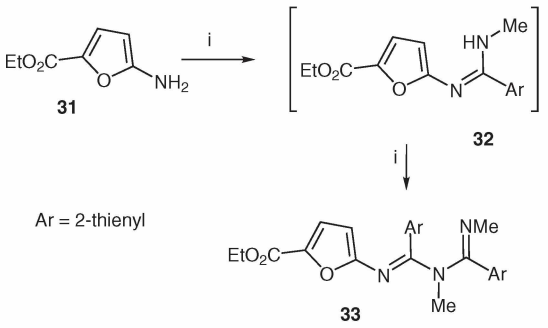


Figure 2 Structure of cyclic phosphine oxide **27**. Selected bond lengths (Å) and angles (°): P(1)–O(1) 1.471(1), P(1)–N(1) 1.717(1), P(1)–N(3) 1.645(2), P(1)–C(3) 1.750(2), S(1)–C(2) 1.732(2), S(1)–C(5) 1.733(2), N(1)–C(1) 1.374(2), N(2)–C(1) 1.304(2), N(2)–C(2) 1.360(2), C(2)–C(3) 1.381(2), C(3)–C(4) 1.421(2), C(4)–C(5) 1.357(3); N(1)–P(1)–C(3) 99.5(1), C(2)–S(1)–C(5) 91.2(1), P(1)–N(1)–C(1) 125.6(1), C(1)–N(2)–C(2) 119.0(1).

Unfortunately, we failed to extend this method to aminofuran derivatives due to the absence of convenient methods for the synthesis of the corresponding NH-amidines. The treatment of aminofuran **31** with an imidoyl chloride in the presence of base does not stop at the formation of amidine **32**, but proceeds further giving compound **33** (Scheme 10).



Scheme 10 *Reagents and conditions:* (i) *N*-methylthiophene-2-carboximidoyl chloride (1 equiv), benzene, 10 °C, 10 h.

We then looked at an alternative strategy starting from formamidines derived from aminothiophene **34** and aminofuran **39** (Scheme 11).[10] Formamidine **34**, contrary to formamidines derived from aminopyrazoles, reacts only with active phosphorylating agents such as phosphorus tribromide. Formamidine **39** reacts both with phosphorous trichloride and phosphorous tribromide, although in the case of phosphorous trichloride two equivalents of the phosphorylating agent is required, which complicates further transformation of the corresponding dichlorophosphine.

Dibromophosphines **35** and **40** were used in situ and were transformed into the corresponding chlorophosphonium chlorides **36** and **41** which, upon further treatment with ammonia solution in dichloromethane gave the diazaphosphinines **38** and **43** (Scheme 11).

^{1}H NMR spectroscopy established the formation of the diazaphosphinine cycle. The presence of two doublets at 8.06 ppm ($^3J_{HP}$ = 44.7 Hz) and 7.59 ppm ($^3J_{HP}$ = 3.9 Hz) for compound **38** and at 7.89 ppm ($^3J_{HP}$ = 48.0 Hz) and 7.44 ppm ($^3J_{HP}$ = 3.0 Hz) for compound **43** were assigned to protons at C3 and C7 corroborating the formation of the fused diazaphosphinine system. The structure of compound **38** was confirmed by single X-ray diffraction (Figure 3).

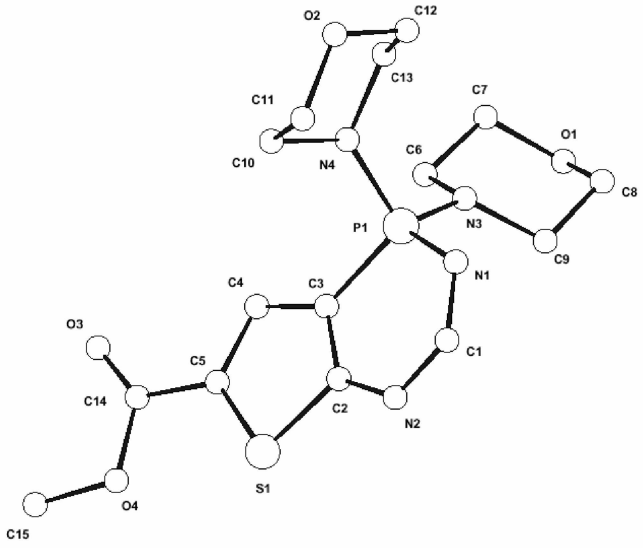
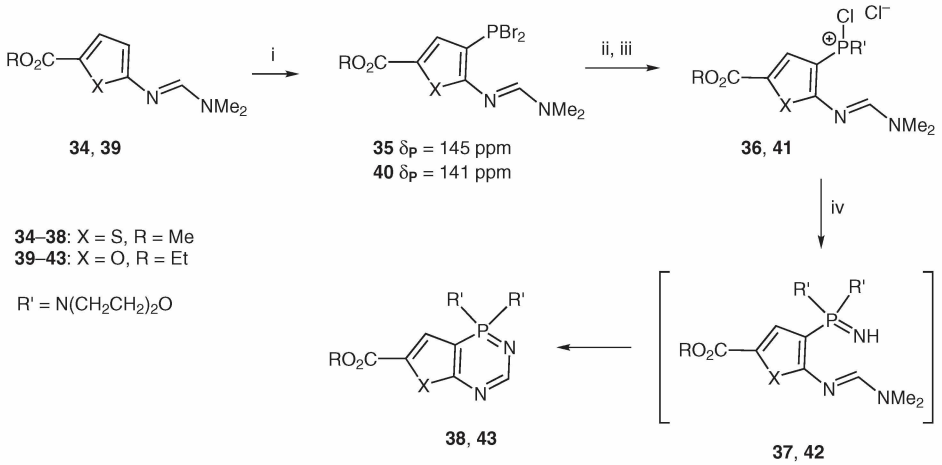


Figure 3 Structure of diazaphosphinine **38**. Selected bond lengths (Å) and angles (°): P(1)–N(1) 1.611(2), P(1)–N(3) 1.642(2), P(1)–N(4) 1.645(2), P(1)–C(3) 1.755(3), S(1)–C(2) 1.745(3), S(1)–C(5) 1.733(2), N(1)–C(1) 1.326(3), N(2)–C(1) 1.329(3), N(2)–C(2) 1.357(3), C(2)–C(3) 1.395(4), C(3)–C(4) 1.413(3), C(4)–C(5) 1.356(3); N(1)–P(1)–C(3) 105.3(1), C(2)–S(1)–C(5) 91.4(1), P(1)–N(1)–C(1) 122.4(2), C(1)–N(2)–C(2) 115.7(2).

In conclusion, we elaborated two general approaches to condensed diazaphosphinines starting from amidines derived from aminoheterocycles. Facile accessibility of starting amidines as well as the one-pot procedures made these methods very attractive for the design and synthesis of fused phospha-pyrimidines with various arrangements of functional groups at the fused diazaphosphinine nuclei.



Scheme 11 *Reagents and conditions:* (i) PBr_3, py, r.t., 12 h; (ii) amine, Et_3N, py, 1 h; (iii) C_2Cl_6, PhH; (iv) NH_3, CH_2Cl_2, 24 h.

Table 1 Analytical Data for Phosphorus Compounds and Starting Amidines[a]

Compd	Yield (%)[b]	Mp (°C)[c]	^{31}P NMR, δ (solvent)	^{1}H NMR, δ
5a	74	250	–	2.10 (s, 3 H, CH_3), 3.03 (d, $^3J_{HH}$ = 4 Hz, 3 H, $NHCH_3$), 4.80 (br s, 1 H, $NHCH_3$), 4.90 (s, 1 H, pyrazole-H), 7.15 (t, $^3J_{HH}$ = 6.3 Hz, 1 H, Ph), 7.19 (t, $^3J_{HH}$ = 7.8 Hz, 1 H, Ph), 7.71 (d, $^3J_{HH}$ = 7.8 Hz, 2 H, Ph), 7.26–7.39 (m, 6 H, Ph)[d]
5b	71	172–173	–	2.21 (s, 3 H, CH_3), 3.01 (d, $^3J_{HH}$ = 4 Hz, 3 H, $NHCH_3$), 5.00 (br s, 1 H, $NHCH_3$), 5.31 (s, 1 H, pyrazole-H), 6.97 (br s, 2 H, Ar), 7.17 (t, $^3J_{HH}$ = 7.8 Hz, 1 H, Ar), 7.26–7.35 (m, 3 H, Ar), 7.60 (d, $^3J_{HH}$ = 7.8 Hz, 2 H, Ar)[d]
11	43	210–211	4.5 (py)	2.38 (s, 3 H, CH_3), 3.46 (d, $^3J_{PH}$ = 8.7 Hz, 3 H, NCH_3), 7.30 (t, $^3J_{HH}$ = 6.3 Hz, 1 H, Ph), 7.43 (t, $^3J_{HH}$ = 7.2 Hz, 2 H, Ph), 7.50–7.56 (m, 3 H, Ph), 7.71–7.74 (m, 2 H, Ph), 7.89 (d, $^3J_{HH}$ = 8.1 Hz, 2 H, Ph)[d]
12a	64	155–160	62 (benzene)	2.53 (s, 3 H, CH_3), 2.60–2.80 [m, 4 H, $N(CH_2CH_2)_2O$], 2.85 (d, $^3J_{PH}$ = 12.3 Hz, 3 H, NCH_3), 3.19 [t, $^3J_{HH}$ = 4.2 Hz, 4 H, $N(CH_2CH_2)_2O$], 6.95 (t, $^3J_{HH}$ = 7.5 Hz, 1 H, Ph), 7.11–7.15 (m, 3 H, Ph), 7.22 (t, $^3J_{HH}$ = 7.5 Hz, 2 H, Ph), 7.44 (dd, $^3J_{HH}$ = 7.5 Hz, $^4J_{HH}$ = 2.1 Hz, 2 H, Ph), 8.67 (d, $^3J_{HH}$ = 9.0 Hz, 2 H, Ph)[f]
14a	82	192	50 (acetone)	2.54 (s, 3 H, CH_3), 3.05–3.18 [m, 2 H, $N(CH_2CH_2)_2O$], 3.15 (d, $^3J_{PH}$ = 8.7 Hz, 3 H, NCH_3), 3.40–3.52 [m, 2 H, $N(CH_2CH_2)_2O$], 3.64 [t, $^3J_{HH}$ = 4.5 Hz, 4 H, $N(CH_2CH_2)_2O$], 7.24 (t, $^3J_{HH}$ = 7.2 Hz, 1 H, Ph), 7.39 (t, $^3J_{HH}$ = 7.2 Hz, 2 H, Ph), 7.44–7.47 (m, 5 H, Ph), 7.92 (d, $^3J_{HH}$ = 7.5 Hz, 2 H, Ph)[d]
14b	76	205–206	50 (acetone)	2.53 (s, 3 H, CH_3), 3.05–3.18 [m, 2 H, $N(CH_2CH_2)O$], 3.48 (d, $^3J_{PH}$ = 8.7 Hz, 3 H, NCH_3), 3.40–3.52 [m, 2 H, $N(CH_2CH_2)O$], 3.62 [t, $^3J_{HH}$ = 4.5 Hz, 4 H, $N(CH_2CH_2)O$], 7.10 (dd, $^3J_{HH}$ = 4.8 Hz, $^3J_{HH}$ = 3.9 Hz, 1 H, Ar), 7.28 (t, $^3J_{HH}$ = 7.5 Hz, 1 H, Ar), 7.42–7.47 (m, 3 H, Ar), 7.50 (t, $^3J_{HH}$ = 4.8 Hz, 1 H, Ar), 7.98 (d, $^3J_{HH}$ = 8.4 Hz, 2 H, Ar)[d]
14c	65	96–97	41 (py)	2.55 (s, 3 H, CH_3), 3.15 (d, $^3J_{PH}$ = 8.7 Hz, 3 H, NCH_3), 5.88 (d, $^2J_{PH}$ = 10.5 Hz, 1 H, NH), 6.26–6.32 (m, 2 H, Ph), 6.66 (dt, $^3J_{HH}$ = $^3J_{FH}$ = 7.9 Hz, $^4J_{HH}$ = 1.5 Hz, 1 H, Ph), 7.13 (m, 1 H, Ph), 7.23–7.34 (m, 3 H, Ph), 7.39–7.44 (m, 5 H, Ph), 7.92 (d, $^3J_{HH}$ = 7.8 Hz, 2 H, Ph)[d]
14d	64	164–165	42 (py)	2.51 (s, 3 H, CH_3), 3.53 (d, $^3J_{PH}$ = 8.7 Hz, 3 H, NCH_3), 6.13 (br d, $^2J_{PH}$ = 9.3 Hz, 1 H, NH), 6.37 (d, $^3J_{HH}$ = 8.1 Hz, 1 H, Ar), 7.03 (t, $^3J_{HH}$ = 7.8 Hz, 1 H, Ar), 7.06 (dd, $^3J_{HH}$ = 4.8 Hz, $^3J_{HH}$ = 3.9 Hz, 1 H, Ar), 7.22 (t, $^3J_{HH}$ = 7.2 Hz, 1 H, Ar), 7.27 (dd, $^3J_{HH}$ = 3.9 Hz, $^4J_{HH}$ = 0.6 Hz, 1 H, Ar), 7.31 (t, $^3J_{HH}$ = 7.2 Hz, 1 H, Ar), 7.47 (t, $^3J_{HH}$ = 7.2 Hz, 2 H, Ar), 7.50 (d, $^3J_{HH}$ = 4.8 Hz, $^4J_{HH}$ = 0.6 Hz, 1 H, Ar), 7.57 (d, $^3J_{HH}$ = 7.8 Hz, 1 H, Ar), 7.98 (d, $^3J_{HH}$ = 7.5 Hz, 2 H, Ar)[d]
15a	85	177	–1.6 (py)	2.43 (s, 3 H, CH_3), 3.03 (d, $^3J_{PH}$ = 6.3 Hz, 3 H, NCH_3), 3.20 [m, 2 H, $N(CH_2CH_2)_2O$], 3.51 [m, 2 H, $N(CH_2CH_2)_2O$], 3.73 [m, 4 H, $N(CH_2CH_2)_2O$], 6.55 (d, $^3J_{HH}$ = 8.7 Hz, 2 H, Ph), 7.28 (t, $^3J_{HH}$ = 7.6 Hz, 1 H, Ph), 7.40–7.51 (m, 7 H, Ph), 7.97 (d, $^3J_{HH}$ = 7.8 Hz, 2 H, Ph), 8.01 (d, $^3J_{HH}$ = 7.8 Hz, 2 H, Ph)[d]
15b	54	168	–1.6 (py)	2.45 (s, 3 H, CH_3), 3.06 (d, $^3J_{PH}$ = 6.3 Hz, 3 H, NCH_3), 3.21 [m, 2 H, $N(CH_2CH_2)_2O$], 3.50 [m, 2 H, $N(CH_2CH_2)_2O$], 3.73 [t, $^3J_{HH}$ = 4.5 Hz, 4 H, $N(CH_2CH_2)_2O$], 6.88 (d, $^3J_{HH}$ = 8.4 Hz, 1 H, Ph), 7.16 (t, $^3J_{HH}$ = 7.8 Hz, 1 H, Ph), 7.26 (t, $^3J_{HH}$ = 7.2 Hz, 1 H, Ph), 7.39–7.44 (m, 3 H, Ph), 7.48 (br s, m, 5 H, Ph), 7.57 (d, $^3J_{HH}$ = 7.8 Hz, 1 H, Ph), 7.98 (d, $^3J_{HH}$ = 7.5 Hz, 2 H, Ph)[d]
15c	87	145–146	1.9 (py)	2.40 (s, 3 H, CH_3), 3.18 [m, 2 H, $N(CH_2CH_2)_2O$], 3.44 (d, $^3J_{PH}$ = 7.2 Hz, 3 H, NCH_3), 3.45 [m, 2 H, $N(CH_2CH_2)_2O$], 3.70 [t, $^3J_{HH}$ = 4.5 Hz, 4 H, $N(CH_2CH_2)_2O$], 6.54 (d, $^3J_{HH}$ = 8.4 Hz, 2 H, Ar), 7.13 (dd, $^3J_{HH}$ = 5.1 Hz, $^3J_{HH}$ = 3.9 Hz, 1 H, Ar), 7.32 (t, 1 H, $^3J_{HH}$ = 7.2 Hz, Ar), 7.46–7.51 (m, 3 H, Ar), 7.57 (d, $^3J_{HH}$ = 5.1 Hz, 1 H, Ar), 7.93 (d, $^3J_{HH}$ = 7.5 Hz, 2 H, Ar), 8.07 (d, $^3J_{HH}$ = 8.4 Hz, 2 H, Ar)[d]
17	85	210–211	11.6 ($CHCl_3$)	2.57 (s, 3 H, CH_3), 3.05 [m, 2 H, $N(CH_2CH_2)_2O$], 3.14 (d, $^3J_{PH}$ = 6.6 Hz, 3 H, NCH_3), 3.31 [m, 2 H, $N(CH_2CH_2)_2O$], 3.68 [t, $^3J_{HH}$ = 4.5 Hz, 4 H, $N(CH_2CH_2)_2O$], 7.25 (t, $^3J_{HH}$ = 7.2 Hz, 1 H, Ph), 7.40 (t, $^3J_{HH}$ = 7.2 Hz, 2 H, Ph), 7.44–7.50 (m, 5 H, Ph), 7.94 (d, $^3J_{HH}$ = 7.5 Hz, 2 H, Ph)[d]
18a	71	130–131	57 (acetone)	2.60 (s, 3 H, CH_3), 3.30 (d, $^3J_{PH}$ = 6.6 Hz, 3 H, NCH_3), 3.73 (d, $^3J_{PH}$ = 15.0 Hz, 3 H, OCH_3), 7.26 (t, $^3J_{HH}$ = 7.2 Hz, 1 H, Ph), 7.41 (t, $^3J_{HH}$ = 7.2 Hz, 2 H, Ph), 7.44–7.50 (m, 5 H, Ph), 7.90 (d, $^3J_{HH}$ = 7.5 Hz, 2 H, Ph)[d]

Table 1 Analytical Data for Phosphorus Compounds and Starting Amidines[a] (continued)

Compd	Yield (%)[b]	Mp (°C)[c]	^{31}P NMR, δ (solvent)	^{1}H NMR, δ
18b	69	122–123	58 (acetone)	1.35 (t, $^{3}J_{HH}$ = 7.2 Hz, 3 H, OCH_2CH_3), 2.59 (s, 3 H, CH_3), 3.30 (d, $^{3}J_{PH}$ = 8.7 Hz, 3 H, NCH_3), 4.11 (m, 2 H, OCH_2CH_3), 7.26 (t, $^{3}J_{HH}$ = 7.2 Hz, 1 H, Ph), 7.40 (t, $^{3}J_{HH}$ = 7.2 Hz, 2 H, Ph), 7.47 (br s, m, 5 H, Ph), 7.89 (d, $^{3}J_{HH}$ = 7.5 Hz, 2 H, Ph)[d]
18c	64	110–111	57 (acetone)	2.58 (s, 3 H, CH_3), 3.66 (d, $^{3}J_{PH}$ = 6.6 Hz, 3 H, NCH_3), 3.68 (d, $^{3}J_{PH}$ = 15.0 Hz, 3 H, OCH_3), 7.11 (dd, $^{3}J_{HH}$ = 4.8 Hz, $^{3}J_{HH}$ = 3.9 Hz, 1 H, Ar), 7.30 (t, $^{3}J_{HH}$ = 7.5 Hz, 1 H, Ar), 7.43–7.54 (m, 4 H), 7.95 (d, $^{3}J_{HH}$ = 8.4 Hz, 2 H, Ar)[d]
18d	73	115–116	57 (acetone)	1.32 (t, $^{3}J_{HH}$ = 7.2 Hz, 3 H, OCH_2CH_3), 2.58 (s, 3 H, CH_3), 3.65 (d, $^{3}J_{PH}$ = 8.7 Hz, 3 H, NCH_3), 4.04 (m, 2 H, OCH_2CH_3), 7.12 (dd, $^{3}J_{HH}$ = 4.8 Hz, $^{3}J_{HH}$ = 3.9 Hz, 1 H, Ar), 7.29 (t, $^{3}J_{HH}$ = 7.5 Hz, 1 H, Ar), 7.43–7.54 (m, 4 H, Ar), 7.95 (d, $^{3}J_{HH}$ = 8.4 Hz, 2 H, Ar)[d]
20a	57	270–271	5.3 (py)	2.22 (s, 3 H, $CH_3C_6H_4NH$), 2.52 (s, 3 H, CH_3), 3.15 (d, $^{3}J_{PH}$ = 8.7 Hz, 3 H, NCH_3), 6.49 (d, $^{3}J_{HH}$ = 8.1 Hz, 2 H, Ph), 6.91 (d, $^{2}J_{PH}$ = 4.5 Hz, 1 H, NH), 6.96 (d, $^{3}J_{HH}$ = 8.1 Hz, 2 H, Ph), 7.27 (t, $^{3}J_{HH}$ = 7.5 Hz, 1 H, Ph), 7.35–7.45 (m, 7 H, Ph), 7.97 (d, $^{3}J_{HH}$ = 7.5 Hz, 2 H, Ph)[d]
20b	59	258–259	5.6 (py)	2.24 [s, 3 H, $CH_3(Cl)C_6H_3NH$], 2.51 (s, 3 H, CH_3), 3.16 (d, $^{3}J_{PH}$ = 6.6 Hz, 3 H, NCH_3), 6.39 (dd, $^{3}J_{HH}$ = 7.8 Hz, $^{4}J_{HH}$ = 2.1 Hz, 1 H, Ph), 6.59 (d, $^{4}J_{HH}$ = 2.1 Hz, 1 H, Ph), 6.98 (d, $^{3}J_{HH}$ = 7.8 Hz, 1 H, CH), 7.28 (t, $^{3}J_{HH}$ = 7.5 Hz, 1 H, Ph), 7.40–7.47 (m, 8 H, Ph, NH), 7.95 (d, $^{3}J_{HH}$ = 7.5 Hz, 2 H, Ph)[d]
20c	72	206–208	5.6 (py)	2.20 [s, 3 H, $CH_3(Cl)C_6H_3NH$], 2.50 (s, 3 H, CH_3), 3.53 (d, $^{3}J_{PH}$ = 9.9 Hz, 3 H, NCH_3), 6.30 (dd, $^{3}J_{HH}$ = 9.0 Hz, $^{4}J_{HH}$ = 3.0 Hz, 1 H, Ar), 6.67 (d, $^{4}J_{HH}$ = 3.0 Hz, 1 H, Ar), 6.93 (d, $^{3}J_{HH}$ = 9.0 Hz, 1 H, Ar), 7.10 (dd, $^{3}J_{HH}$ = 4.8 Hz, $^{3}J_{HH}$ = 3.9 Hz, 1 H, Ar), 7.32 (t, $^{3}J_{HH}$ = 7.5, 1 H, Ar), 7.41–7.54 (m, 4 H, Ar), 7.70 (br d, $^{2}J_{PH}$ = 7.8 Hz, 1 H, NH), 8.02 (d, $^{3}J_{HH}$ = 9.0 Hz, 2 H, Ar)[d]
21a	73	192–194	27 ($CHCl_3$)	2.34 (s, 3 H, CH_3-furyl), 2.37 (s, 3 H, CH_3), 3.53 (d, $^{3}J_{PH}$ = 9.3 Hz, 3 H, NCH_3), 6.17 (m, 1 H, Ar), 7.22–7.31 (m, 2 H, Ar), 7.40 (t, $^{3}J_{HH}$ = 7.2 Hz, 2 H, Ar), 7.46–7.51 (m, 5 H, Ar), 7.89 (d, $^{3}J_{HH}$ = 7.5 Hz, 2 H, Ar)[d]
21b	75	155–156	27 ($CHCl_3$)	2.30 (s, 3 H, CH_3-furyl), 2.35 (s, 3 H, CH_3), 3.43 (d, $^{3}J_{PH}$ = 9.0 Hz, 3 H, NCH_3), 6.16 (m, 1 H, Ar), 7.09 (dd, $^{3}J_{HH}$ = 4.8 Hz, $^{3}J_{HH}$ = 3.9 Hz, 1 H, Ar), 7.29–7.31 (m, 2 H, Ar), 7.43–7.52 (m, 4 H, Ar), 7.99 (d, $^{3}J_{HH}$ = 7.5 Hz, 2 H, Ar)[d]
22	47	133–134	–	2.88 (d, $^{3}J_{HH}$ = 4.5 Hz, 3 H, $NHCH_3$), 3.65 (s, 3 H, OCH_3), 6.06 (d, $^{3}J_{HH}$ = 3.9 Hz, 1 H, thiophene-H), 7.30–7.36 (m, 3 H, Ar), 7.41–7.45 (m, 3 H, CH), 7.88 (br q, $^{3}J_{HH}$ = 4.5 Hz, 1 H, NH)[e]
25	68	143–144	48 (py)	2.88 (d, $^{3}J_{HH}$ = 8.9 Hz, 3 H, NCH_3), 3.80 (s, 3 H, OCH_3), 7.54–7.57 (m, 6 H, Ar), 7.64–7.69 (m, 3 H, Ar), 7.91 (ddd, $^{3}J_{HP}$ = 15.6 Hz, $^{3}J_{HH}$ = 7.8 Hz, $^{4}J_{HH}$ = 1.5 Hz, 2 H, Ar)[d]
27	40	193–194	9.0 (py)	2.99 [2 H, m, $N(CH_2CH_2)_2O$], 3.15 (d, $^{3}J_{HH}$ = 6.6 Hz, 3 H, NCH_3), 3.26 [m, 2 H, $N(CH_2CH_2)_2O$], 3.92 (s, 3 H, OCH_3), 3.65 [m, 4 H, $N(CH_2CH_2)_2O$], 7.43–7.52 (m, 5 H, Ph), 7.95 (d, $^{3}J_{HP}$ = 5.7 Hz, 1 H, thiophene-H)[d]
28	63	198–199	52.8 (py)	3.03 [m, 2 H, $N(CH_2CH_2)_2O$], 3.08 (d, $^{3}J_{HH}$ = 8.7 Hz, 3 H, NCH_3), 3.33 [m, 2 H, $N(CH_2CH_2)_2O$], 3.53 [m, 4 H, $N(CH_2CH_2)_2O$], 3.85 (s, 3 H, OCH_3), 7.54 (m, 5 H, Ph), 7.83 (d, $^{3}J_{HP}$ = 5.7 Hz, 1 H, thiophene-H)[d]
30a	65	272–273	9 (py)	2.99 (d, $^{3}J_{HH}$ = 4.8 Hz, 3 H, $NHCH_3$), 3.64 (s, 3 H, OCH_3), 3.73 [m, 4 H, $N(CH_2CH_2)_2O$], 3.46 [m, 4 H, $N(CH_2CH_2)_2O$], 7.07 (d, $^{3}J_{HH}$ = 8.7 Hz, 2 H, Ph), 7.17 (d, $^{3}J_{HH}$ = 8.7 Hz, 2 H, Ph), 7.30 (d, $^{3}J_{HH}$ = 8.7 Hz, 2 H, Ph), 7.39 (t, $^{3}J_{HH}$ = 7.6 Hz, 2 H, Ph), 7.49 (t, $^{3}J_{HH}$ = 7.8 Hz, 1 H, Ph), 7.56 (d, $^{3}J_{HH}$ = 5.7 Hz, 1 H, thiophene-H), 7.78 (d, $^{3}J_{HP}$ = 11.7 Hz, 1 H, PNH), 8.29 (br q, $^{3}J_{HH}$ = 4.8 Hz, 1 H, $NHCH_3$)[e]
30b	66	246–247	10 (py)	2.23 (s, 3 H, CH_3), 3.00 (d, $^{3}J_{HH}$ = 3.9 Hz, 3 H, $NHCH_3$), 3.14 [m, 4 H, $N(CH_2CH_2)_2O$], 3.46 [m, 4 H, $N(CH_2CH_2)_2O$], 3.64 (s, 3 H, OCH_3), 6.96 (d, $^{3}J_{HH}$ = 8.7 Hz, 1 H, Ph), 7.10 (d, $^{3}J_{HH}$ = 8.4 Hz, 1 H, Ph), 7.19–7.22 (m, 3 H, Ph), 7.39 (t, $^{3}J_{HH}$ = 6.9 Hz, 2 H, Ph), 7.49 (t, $^{3}J_{HH}$ = 7.8 Hz, 1 H, Ph), 7.56 (d, $^{3}J_{HH}$ = 5.7 Hz, Ph, thiophene-H), 7.72 (d, $^{3}J_{HP}$ = 11.7 Hz, 1 H, PNH), 8.29 (br q, $^{3}J_{HH}$ = 4.8 Hz, 1 H, $NHCH_3$)[e]

Table 1 Analytical Data for Phosphorus Compounds and Starting Amidines[a] (continued)

Compd	Yield (%)[b]	Mp (°C)[c]	^{31}P NMR, δ (solvent)	^{1}H NMR, δ
33	27	133–134	–	1.34 (t, $^{3}J_{HP}$ = 7.5 Hz, 3 H, CH_3CH_2O), 3.31 (s, 3 H, NCH_3), 3.40 (s, 3 H, NCH_3), 4.31 (q, $^{3}J_{HP}$ = 7.5 Hz, 2 H, CH_3CH_2O), 4.93 (d, $^{3}J_{HH}$ = 3.9 Hz, 1 H, furan-H), 6.85 (t, $^{3}J_{HH}$ = 3.6 Hz, 1 H, thiophene-H), 6.91 (d, $^{3}J_{HH}$ = 3.3 Hz, 1 H, thiophene-H), 6.98 (d, $^{3}J_{HH}$ = 3.9 Hz, 1 H, furan-H), 7.04 (dd, $^{3}J_{HH}$ = 4.5 Hz, 1 H, thiophene-H), 7.30 (d, $^{3}J_{HH}$ = 5.1 Hz, 1 H, thiophene-H), 7.35–7.37 (m, 2 H, thiophene-H)[d]
35	95	82–83	–	2.95 [s, 3 H, $N(CH_3)_2$], 3.08 [s, 3 H, $N(CH_3)_2$], 3.75 (s, 3 H, $COOCH_3$), 6.44 (d, $^{3}J_{HH}$ = 4.2 Hz, 1 H, thiophene-H), 7.53 (d, $^{3}J_{HH}$ = 4.2 Hz, 1 H, thiophene-H), 7.98 (s, 1 H, N=CHN)[e]
38	45	172–173	25 ($CHCl_3$)	3.09 [m, 8 H, $N(CH_2CH_2)_2O$], 3.66 (m, 8 H, $N(CH_2CH_2)_2O$), 3.91 (s, 3 H, CH_3O), 7.60 (d, $^{3}J_{HP}$ = 3.9 Hz, 1 H, thiophene-H), 8.06 (d, $^{3}J_{HP}$ = 44.7 Hz, 1 H, N=CHN)[d]
39	80	115–116	–	1.35 (t, $^{3}J_{HH}$ = 7.2 Hz, 3 H, CH_3CH_2O), 3.05 [s, 3 H, $N(CH_3)_2$], 3.10 [s, 3 H, $N(CH_3)_2$], 4.31 (q, $^{3}J_{HH}$ = 7.2 Hz, 2 H, CH_3CH_2O), 5.70 (d, $^{3}J_{HH}$ = 3.6 Hz, 1 H, furan-H), 7.14 (d, $^{3}J_{HH}$ = 3.3 Hz, 1 H, furan-H), 8.14 (s, 1 H, N=CHN)[d]
43	46	142–143	30 (acetone)	1.34 (t, $^{3}J_{HH}$ = 7.2 Hz, 3 H, CH_3CH_2O), 3.12 [m, 8 H, $N(CH_2CH_2)_2O$], 3.61 [m, 8 H, $N(CH_2CH_2)_2O$], 4.32 (q, $^{3}J_{HH}$ = 7.2 Hz, 2 H, CH_3CH_2O), 7.44 (d, $^{3}J_{HP}$ = 3 Hz, 1 H, furan-H), 8.14 (d, $^{3}J_{HP}$ = 48 Hz, 1 H, N=CHN)[g]

[a] Satisfactory microanalysis obtained: N ± 0.21, P ± 0.13.
[b] Yields refer to pure isolated products.
[c] Melting points are uncorrected.
[d] $CDCl_3$.
[e] DMSO-d_6.
[f] Benzene- d_6.
[g] Acetone-d_6.

All procedures with compounds sensitive to hydrolysis or oxidation were carried out under an atmosphere of dry argon. All solvents were purified and dried by standard methods. Petroleum ether with a bp range 70–110 °C was used. ^{1}H and ^{31}P NMR spectra were recorded on a Varian VXR-300 spectrometer (Table 1) and ^{13}C NMR spectra were recorded on a Varian Mercury-400 spectrometer; ^{1}H and ^{13}C spectra were recorded at 300 and 100 MHz, respectively, with TMS as an internal standard; ^{31}P spectra were recorded at 121 MHz with 85% H_3PO_4 as an external standard. MS were obtained on a 'Hewlett-Packard' HP GC/MS 5890/5972 instrument (EI, 70 eV) by GC inlet or on a MX-1321 instrument (EI, 70 eV) by direct inlet.

Commercially unavailable aminoheterocycles (1-phenyl-3-methyl-5-aminopyrazole,[11a] methyl 5-aminothiophene-2-carboxylate,[11b] and ethyl 5-amino-2-furoate **31**[11b]) and 5-methyl-2-furyldibromophosphine[12] were synthesized according to literature procedures. Experimental details and spectral data for compounds **4a** and **4b** have been reported previously.[6]

N-Methyl-*N*′-(3-methyl-1-phenyl-1*H*-pyrazol-5-yl)aryl(hetaryl)carboximidamides (5a and 5b); General Procedure

To a stirred solution of 1-phenyl-3-methyl-5-aminopyrazole (1.73 g, 0.01 mol) and Et_3N (1.53 mL, 0.011 mol) in CH_2Cl_2 (30 mL) at 0 °C a solution of the corresponding imidoyl chloride (0.01 mol) in CH_2Cl_2 (30 mL) was added. The reaction mixture was left to stand for 1 h at r.t. and then heated at 40 °C for 4 h. The solvent was evaporated in vacuo and the residue was triturated with H_2O and crystallized from dioxane–DMF (ca. 3:1).

5a
MS (EI): *m*/*z* (%) = 291 (16, [M$^+$ + 1]), 290 (77, [M$^+$]), 145 (15), 118 (100, [PhC$^+$=NMe]), 104 (37), 77 (47), 51 (11).

5b
MS (EI): *m*/*z* (%) = 297 (19, [M$^+$ + 1]), 296 (98, [M$^+$]), 254 (11), 124 (100, [2-thienylC$^+$=NMe]), 110 (53), 77 (20), 39 (14).

3-(Het)aryl-1-bromo-2,7-dimethyl-5-phenyl-2,5-dihydro-1*H*-pyrazolo[4,3-*c*][1,5,2]diazaphosphinines (8a and 8b); General Procedure

To a stirred solution of **5** (2 mmol) in anhyd pyridine (20 mL), PBr_3 (0.19 mL, 2 mmol) was added, and stirring was continued for 3 h. The progress of the reaction was monitored by ^{31}P NMR spectroscopy; when the reaction was complete only one signal at 121 ppm was observed. The crude reaction mixture could be used directly in the next step.

3-(Het)aryl-2,7-dimethyl-1-(5-methylthien-2-yl)-5-phenyl-2,5-dihydro-1*H*-pyrazolo[4,3-*c*][1,5,2]diazaphosphinines (9a and 9b); General Procedure

Prepared from **5** and 5-methyl-2-furyldibromophosphine using the general procedure described for **8**. The progress of the reaction was monitored by ^{31}P NMR spectroscopy; when the reaction was complete only one signal at 0.4 ppm was observed.

2,7-Dimethyl-3,5-diphenyl-2,5-dihydro-1*H*-pyrazolo[4,3-*c*][1,5,2]diazaphosphinic Acid (11)

A solution of compound **8a** (2 mmol) in anhyd pyridine (20 mL) was left to stand in the air at r.t. for 48 h. The progress of the reaction was monitored by ^{31}P NMR spectroscopy; after 12 h the dominant signal was at 1.9 ppm (d, $^{1}J_{PH}$ = 600 Hz), corresponding to compound **10**; after 48 h the dominant signal was at 4.5 ppm (s), corresponding to compound **11**. After completion of the reaction pyridine was evaporated in vacuo and the residue was triturated with H_2O and crystallized from *i*-PrOH.

^{13}C NMR (DMSO-d_6): δ = 14.0 (CH_3), 33.5 (NCH_3), 92.6 ($^{1}J_{CP}$ = 186.5 Hz, C7a), 123.6 (N5-*o*-Ph), 127.7 (N5-*p*-Ph), 128.8

(N5-*m*-Ph), 129.2 (C3-*m*-Ph), 129.5 (C3-*o*-Ph), 131.0 (C3-*o*-Ph), 135.3 ($^3J_{CP}$ = 4.8 Hz, C3-*i*-Ph), 138.3 (N5-*i*-Ph), 147.8 ($^2J_{CP}$ = 9.6 Hz, C4a), 152.1 ($^2J_{CP}$ = 9.3 Hz, C7), 160.9 (C3)

MS (EI, TMS ester derivative): *m/z* (%) = 425 (28, [M$^+$ + 1]), 424 (100, [M$^+$]), 423 (51), 409 (29), 407 (15), 118 (56, [PhC$^+$=NMe]), 77 (39).

2,7-Dimethyl-1-morpholin-4-yl-3,5-diphenyl-2,5-dihydro-1*H*-pyrazolo[4,3-*c*][1,5,2]diazaphosphinine (12a)

To a stirred solution of compound **8a** (4 mmol) in anhyd pyridine (40 mL), morpholine (0.35 mL, 4 mmol) was added. The reaction mixture was left to stand for 10 min at r.t. and then pyridine was carefully evaporated in vacuo. Anhyd benzene (20 mL) was added to the residue and the resulting solution was heated to 50 °C. The precipitated py·HBr was removed by filtration at 50 °C under an atmosphere of dry argon. The benzene solution was cooled to r.t. and then heptane (10 mL) was added. The target amide **12a** precipitated, was removed by filtration, and dried in vacuo.

1-Amido-3-(Het)aryl-2,7-dimethyl-5-phenyl-2,5-dihydro-1*H*-pyrazolo[4,3-*c*][1,5,2]diazaphosphinine 1-Thioxides (14); General Procedure

To a stirred solution of compound **8** (5 mmol) in pyridine (20 mL), amine (5 mmol) and S (5 mmol) were added. After complete dissolution of S, pyridine was evaporated in vacuo. The residue was triturated with H_2O and crystallized from *i*-PrOH.

14a

MS (EI): *m/z* (%) = 437 (30, [M$^+$]), 352 (15), 351 (22, [M$^+$ – N(CH$_2$CH$_2$)$_2$O]), 320 (19), 319 (100, [M$^+$ – N(CH$_2$CH$_2$)$_2$O – S]), 118 (23, [PhC$^+$=NMe]), 77 (20), 60 (76).

3-(Het)aryl-2,7-dimethyl-1-morpholin-4-yl-5-phenyl-2,5-dihydro-1*H*-1λ^5-pyrazolo[4,3-*c*][1,5,2]diazaphosphinine 1-Arylimides (15); General Procedure

To a stirred solution of compound **8** (5 mmol) in pyridine (20 mL), secondary amine (5 mmol), and arylazide (5 mmol) were added. The mixture was maintained at 50 °C until nitrogen evolution had ceased and then pyridine was evaporated in vacuo. The residue was triturated with H_2O and crystallized from *i*-PrOH.

15a

MS (EI): *m/z* (%) = 541 (13, [M$^+$]), 320 (19), 319 (100, [M$^+$ – N(CH$_2$CH$_2$)$_2$O – 4-NO$_2$C$_6$H$_4$N]), 118 (24, [PhC$^+$=NMe]).

2,7-Dimethyl-1-morpholin-4-yl-3,5-diphenyl-2,5-dihydro-1*H*-pyrazolo[4,3-*c*][1,5,2]diazaphosphinine 1-Oxide (17)

To a stirred solution of amide **12** (810 mg, 2 mmol) in toluene (40 mL), Br_2 (320 mg, 2 mmol) was added at 0 °C. The reaction mixture was left to stand for 10 min at r.t. and then treated with an aq solution of $NaHCO_3$ (20 mL). The organic layer was separated, washed with H_2O (2 × 40 mL), and dried over Na_2SO_4. The toluene was evaporated in vacuo and the residue was crystallized from *i*-PrOH.

15a

^{13}C NMR (DMSO-d_6): δ = 14.4 (CH$_3$), 32.5 (NCH$_3$), 44.3 [N(CH$_2$CH$_2$)$_2$O], 67.2 [$^3J_{CP}$ = 7.6 Hz, N(CH$_2$CH$_2$)$_2$O], 92.3 ($^1J_{CP}$ = 186.5 Hz, C7a), 122.9 (N5-*o*-Ph), 127.0 (N5-*p*-Ph), 128.5 (N5-*m*-Ph), 129.0 (C3-*m*-Ph), 129.4 (C3-*o*-Ph), 130.2 (C3-*o*-Ph), 136.4 ($^3J_{CP}$ = 4.8 Hz, C3-*i*-Ph), 139.0 (N5-*i*-Ph), 147.8 ($^2J_{CP}$ = 9.6 Hz, C4a), 152.1 ($^2J_{CP}$ = 9.3 Hz, C7), 160.8 (C3).

MS (EI): *m/z* (%) = 422 (19, [M$^+$ + 1]), 421 (93, [M$^+$]), 336 (100, [M$^+$ – N(CH$_2$CH$_2$)$_2$O + H]), 335 (74, [M$^+$ – N(CH$_2$CH$_2$)$_2$O]), 118 (84, [PhC$^+$=NMe]), 86 (19), 77 (48), 60 (17).

1-Alkoxy-3-(Het)aryl-2,7-dimethyl-5-phenyl-2,5-dihydro-1*H*-pyrazolo[4,3-*c*][1,5,2]diazaphosphinine 1-Thioxides (18); Typical Procedure

To a stirred solution of compound **8** (5 mmol) in pyridine (20 mL), alcohol (5 mmol) and S (5 mmol) were added. After complete dissolution of S, pyridine was evaporated in vacuo. The residue was triturated with H_2O and crystallized from *i*-PrOH.

18b

^{13}C NMR (CDCl$_3$): δ = 14.0 (CH$_3$), 16.3 ($^3J_{CP}$ = 6.5 Hz, OCH$_2$CH$_3$), 33.7 ($^2J_{CP}$ = 6.2 Hz, NCH$_3$), 63.9 ($^2J_{CP}$ = 8.9 Hz), 95.5 ($^1J_{CP}$ = 160.7 Hz, C7a), 122.9 (N5-*o*-Ph), 126.6 (N5-*p*-Ph), 127.9 (N5-*m*-Ph), 128.6 (C3-*m*-Ph), 128.8 (C3-*o*-Ph), 130.0 (C3-*o*-Ph), 136.1 ($^3J_{CP}$ = 4.4 Hz, C3-*i*-Ph), 138.5 (N5-*i*-Ph), 148.4 ($^2J_{CP}$ = 11.9 Hz, C4a), 148.6 ($^2J_{CP}$ = 14.8 Hz, C7), 159.6 (C3).

MS (EI): *m/z* (%) = 397 (23, [M$^+$ + 1]), 396 (100, [M$^+$]), 395 (16), 349 (12), 335 (37, [M$^+$ – C$_2$H$_4$ – SH]), 319 (52, [M$^+$ – EtO – S]), 118 (75, [PhC$^+$=NMe]), 77 (56), 60 (19).

1-Anilido-3-(het)aryl-2,7-dimethyl-5-phenyl-2,5-dihydro-1*H*-pyrazolo[4,3-*c*][1,5,2]diazaphosphinine 1-Oxides (20)

To a stirred solution of compound **8** (2 mmol) in pyridine (30 mL), anhyd MeOH (0.08 mL, 2 mmol) and arylazide (2 mmol) were added. The mixture was maintained at 50 °C until nitrogen evolution had ceased and then pyridine was evaporated in vacuo. The residue was triturated with H_2O and crystallized from *i*-PrOH.

20a

MS (EI): *m/z* (%) = 442 (20, [M$^+$ + 1]), 441 (83, [M$^+$]), 336 (20), 335 (100, [M$^+$– 4-MeC$_6$H$_4$NH]), 118 (27, [PhC$^+$=NMe]), 77 (28).

3-(Het)aryl-2,7-dimethyl-1-(5-methyl-2-furyl)-5-phenyl-2,5-dihydro-1*H*-pyrazolo[4,3-*c*][1,5,2]diazaphosphinine 1-Thioxides (21); General Procedure

To a stirred solution of cyclic phosphine **9** (5 mmol) in pyridine (20 mL), S (5 mmol) was added. After complete dissolution of S, pyridine was evaporated in vacuo. The residue was triturated with H_2O and crystallized from *i*-PrOH.

21a

MS (EI): *m/z* (%) = 433 (21, [M$^+$ + 1]), 432 (100, [M$^+$]), 320 (10), 319 (79, [M$^+$ – 5-Me-furyl – S]), 118 (69, [PhC$^+$=NMe]), 77 (64), 60 (19).

Methyl 5-{[(Methylamino)(phenyl)methylene]amino}thiophene-2-carboxylate (22)

To a stirred solution of methyl 5-aminothiophene-2-carboxylate (1.57 g, 0.01 mol) and Et$_3$N (1.53 mL, 0.011 mol) in benzene (30 mL) at 10 °C a solution of the *N*-methylbenzenecarboximidoyl chloride (1.53 g, 0.01 mol) in benzene (10 mL) was added. The reaction mixture was left to stand for 12 h at r.t. The precipitated Et$_3$N·HCl formed was removed by filtration and benzene was evaporated in vacuo. The residue was crystallized from EtOH.

MS (EI): *m/z* (%) = 274 (56, [M$^+$]), 214 (11), 118 (100, [PhC$^+$=NMe]), 104 (34), 77 (35).

1-Bromo-6-carbomethoxy-2-methyl-3-phenyl-1,2-dihydrothieno[3,2-*c*][1,5,2]diazaphosphinine (23)

Compound **23** was prepared from **22** and PBr_3 using the procedure described for **8**. The progress of the reaction was monitored by ^{31}P NMR spectroscopy; when the reaction was complete only one signal at 107 ppm was observed.

6-Carbomethoxy-2-methyl-1,3-diphenyl-1,2-dihydrothieno[3,2-*c*][1,5,2]diazaphosphinine (24)

Compound **24** was prepared from **22** and $PhPBr_2$ using the procedure described for **8**. The progress of the reaction was monitored by

^{31}P NMR spectroscopy; when the reaction was complete only one signal at 35 ppm was observed.

6-Carbomethoxy-2-methyl-1,3-diphenyl-1,2-dihydrothieno[3,2-*c*][1,5,2]diazaphosphinine 1-Thioxide (25)
Compound **25** was prepared from **24** using the procedure described for **21**.

MS (EI): *m/z* (%) = 413 (19, [M$^+$ + 1]), 412 (100, [M$^+$]), 411 (58), 118 (72, [PhC$^+$=NMe]), 77 (46), 60 (21).

6-Carbomethoxy-2-methyl-1-morpholin-4-yl-3-phenyl-1,2-dihydrothieno[3,2-*c*][1,5,2]diazaphosphinine 1-Oxide (27)
To a stirred solution of acid bromide **23** (4 mmol) in anhyd pyridine (40 mL), morpholine (0.35 mL, 4 mmol) was added. The reaction mixture was left to stand for 10 min at r.t. and then pyridine was carefully evaporated in vacuo. Anhyd benzene (20 mL) was added to the residue and the resulting solution was heated to 50 °C. The precipitated Py·HBr was removed by filtration at 50 °C under dry argon. The filtrate contained a solution of amide **26** (^{31}P NMR spectroscopy of the filtrate revealed only one signal at 61 ppm), 30% aq H_2O_2 (2.5 mL) was added, and the reaction mixture was maintained at r.t. for 5 h. The organic layer was separated, washed with H_2O (2 × 15 mL), and dried over Na_2SO_4. Benzene was evaporated in vacuo and the residue was crystallized from *i*-PrOH.

^{13}C NMR (DMSO-d_6): δ = 32.8 ($^2J_{CP}$ = 1.8 Hz, NCH_3), 44.7 [$N(CH_2CH_2)_2O$], 52.8 (CO_2CH_3), 67.5 [$^3J_{CP}$ = 5.3 Hz, $N(CH_2CH_2)_2O$], 112.3 ($^1J_{CP}$ = 167.9 Hz, C7a), 128.0 (*m*-Ph), 129.2 (*o*-Ph), 129.5 ($^2J_{CP}$ = 19.7 Hz, C6), 130.5 (*o*-Ph), 131.3 ($^2J_{CP}$ = 13.7 Hz, C7), 135.6 ($^3J_{CP}$ = 5.7 Hz, *i*-Ph), 160.5 (C3), 162.4 (CO_2CH_3), 167.5 ($^2J_{CP}$ = 10.9 Hz, C4a).

MS (EI): *m/z* (%) = 406 (14, [M$^+$ + 1]), 405 (100, [M$^+$]), 321 (15), 320 (76, [M$^+$ – $N(CH_2CH_2)_2O$ + H]), 319 (78, [M$^+$ – $N(CH_2CH_2)_2O$]),118 (84, [PhC$^+$=NMe]), 86 (44), 77 (33), 60 (57). 54 (14).

6-Carbomethoxy-2-methyl-1-morpholin-4-yl-3-phenyl-1,2-dihydrothieno[3,2-*c*][1,5,2]diazaphosphinine 1-Thioxide (28)
Compound **28** was prepared from acid bromide **23** using the procedure described for **14**.

MS (EI): *m/z* (%) = 421 (28, [M$^+$]), 336 (18, [M$^+$ – $N(CH_2CH_2)_2O$ + H]), 335 (12, [M$^+$ – $N(CH_2CH_2)_2O$]), 304 (13), 303 (100, [M$^+$ – $N(CH_2CH_2)_2O$ – S]), 171 (17), 143 (14), 142 (10), 118 (27, [PhC$^+$=NMe]), 102 (22), 97 (11), 77 (16), 69 (17), 60 (56).

4-{[Arylamino](morpholin-4-yl)phosphoryl}-2-carbomethoxy-5-{[(methylamino)(phenyl)methylene]amino}thiophene (30)
Compounds **30** were prepared from acid bromide **23** using the above procedure for **15**.

30a
^{13}C NMR (DMSO-d_6): δ = 28.8 (NCH_3), 43.7 [$N(CH_2CH_2)_2O$], 51.7 (CO_2CH_3), 66.3 [$^2J_{CP}$ = 5.3 Hz, $N(CH_2CH_2)_2O$], 111.9 (*p*-Ar), 119.0 ($^1J_{CP}$ = 171.8 Hz, thiophene-C4), 119.7 ($^3J_{CP}$ = 5.7 Hz, thiophene-C2), 119.8 (*o*-Ar), 128.6 (*m*-Ar), 128.8 (*m*-Ph), 130.7 (*p*-Ph), 131.5 (*o*-Ph), 131.7 (*i*-Ph), 136.7 ($^2J_{CP}$ = 13.0 Hz, thiophene-C3), 141.2 (*i*-Ar), 161.4 [CO_2CH_3, N=C(Ph)NHMe], 166.1 ($^2J_{CP}$ = 10.7 Hz, thiophene-C5).

MS (EI): *m/z* (%) = 578 (1, [M$^+$]), 118 (100, [PhC$^+$=NMe]).

30b
MS (EI): *m/z* (%) = 546 (2, [M$^+$]), 118 (100, [PhC$^+$=NMe]).

Methyl 5-{[(1*E*)-(Dimethylamino)methylene]amino}thiophene-2-carboxylate (34)
A stirred mixture of methyl 5-aminothiophene-2-carboxylate (5 g, 0.032 mol) and DMF-DMA (10 mL) was heated at 80 °C and the evolved MeOH was collected. After the evolution of MeOH had ceased the excess of DMF-DMA was evaporated in vacuo and the residue was crystallized from PE.

MS (EI): *m/z* (%) = 212 (100, [M$^+$]), 181 (24), 170 (31), 152 (21), 44 (63), 42 (63).

2-Carbomethoxy-4-(dibromophosphino)-5-{[(dimethylamino)methylene]amino}thiophene (35)
To a stirred solution of amidine **34** (2.12 g, 10 mmol) and Et_3N (1.53 mL, 11 mmol) in benzene (40 mL) at 10 °C, PBr_3 (0.95 mL, 10 mmol) was added. The reaction was stirred at r.t. for 12 h. The progress of the reaction was monitored by ^{31}P NMR spectroscopy; when the reaction was complete only one signal at 145 ppm was observed. The crude reaction mixture could be used directly in the next step.

6-Carbomethoxy-1,1-dimorpholin-4-yl-1λ^5-thieno[3,2-*c*][1,5,2]diazaphosphinine (38)
Morpholine (3.95 mL, 45 mmol) in benzene (40 mL) was added at 10 °C to a stirred solution of dibromophosphine **35** (10 mmol) and the reaction mixture was maintained at r.t. for 2 h. The precipitated morpholine hydrobromide formed was removed by filtration. Then a solution of C_2Cl_6 (2.37 g, 10 mmol) in benzene (10 mL) was added to the filtrate. After 12 h the precipitated chlorophosphonium chloride **36** was removed by filtration and dissolved in CH_2Cl_2 (30 mL). The solution of **36** was saturated with dry gaseous NH_3 and the reaction mixture was left to stand for 24 h at r.t. The precipitated NH_4Cl formed was removed by filtration, CH_2Cl_2 was evaporated in vacuo, and the residue was crystallized from a mixture of benzene–heptane.

^{13}C NMR ($CDCl_3$): δ = 44.2 [$N(CH_2CH_2)_2O$], 52.4 (CO_2CH_3), 66.7 [$^3J_{CP}$ = 6.4 Hz, $N(CH_2CH_2)_2O$], 99.7 ($^1J_{CP}$ = 126.0 Hz, C7a), 125.2 ($^3J_{CP}$ = 19.1 Hz, C6), 129.4 ($^2J_{CP}$ = 7.5 Hz, C7), 159.4 ($^2J_{CP}$ = 9.4 Hz, C3), 162.4 (CO_2CH_3), 172.9 ($^3J_{CP}$ = 10.0 Hz, C4a).

MS (EI): *m/z* (%) = 385 (11, [M$^+$ + 1]), 384 (67, [M$^+$]), 328 (14), 327 (100, [M$^+$ – CH_3O – CO]), 298 (13), 242 (24), 214 (15), 213 (77, [M$^+$ – 2 $N(CH_2CH_2)_2O$ + H]), 87 (50), 86 (96), 59 (13), 57 (18), 56 (48), 42 (13).

Ethyl 5-{[(1*E*)-(Dimethylamino)methylene]amino}-2-furoate (39)
Compound **39** was prepared from 5-amino-2-furoate using the procedure described for **34**.

MS (EI): *m/z* (%) = 210 (71, [M$^+$]), 153 (17), 109 (12), 108 (15), 57 (31), 44 (20), 42 (100).

2-Carboethoxy-4-(dibromophosphino)-5-{[(dimethylamino)methylene]amino}furan (40)
Compound **40** was prepared from amidine **39** using the procedure described for **35**. The progress of the reaction was monitored by ^{31}P NMR spectroscopy; when the reaction was complete only one signal at 141 ppm was observed.

6-Carboethoxy-1,1-dimorpholin-4-yl-1λ^5-furo[3,2-*c*][1,5,2]diazaphosphinine (43)
Compound **43** was prepared from dibromophosphine **40** using the procedure described for **38**.

^{13}C NMR ($CDCl_3$): δ = 14.5 ($CO_2CH_2CH_3$), 44.2 [$N(CH_2CH_2)_2O$], 62.4 ($CO_2CH_2CH_3$), 66.7 [$^3J_{CP}$ = 6.4 Hz, $N(CH_2CH_2)_2O$], 83.4 ($^1J_{CP}$ = 126.0 Hz, C7a), 114.2 ($^2J_{CP}$ = 7.5 Hz, C7), 138.4

Table 2 Crystal Data and Structure Refinement Parameters for Compounds **27** and **38**[15]

	27	**38**
Empirical formula	$C_{18}H_{20}N_3O_4P$	$C_{15}H_{21}N_4O_4PS$
Cell parameters:		
a (Å)	8.337(4)	16.605(8)
b (Å)	10.272(3)	11.442(9)
c (Å)	11.396(2)	18.904(6)
α (°)	102.29(2)	90.0
β (°)	90.18(3)	90.0
γ (°)	94.80(3)	90.0
V (Å^3)	949.8(7)	3592(3)
Z	2	8
D_{calcd} (gcm^{-3})	1.42	1.42
Crystal system	triclinic	orthorhombic
Space group	P1 (N2)	Pbca
μ (cm^{-1})	2.74	2.86
Molecular weight	405.41	384.39
F(000)	1365.8	1703.4
Crystal shape	block	sphere
Crystal size (mm)	0.34 × 0.56 × 0.65	0.56 × 0.56 × 0.56
Index ranges	$0 \le h \le 10$ $-13 \le k \le 13$ $-14 \le l \le 14$	$0 \le h \le 18$ $0 \le k \le 12$ $0 \le l \le 21$
θ_{max} (°)	27	30
No of reflections:		
Collected	4151	3092
Unique	4137	2724
in refinement	3228 [I > 3σ(I)]	2028 [I > 3σ(I)]
No of refined parameters	244	226
Obs./var.	13.2	9.0
Final R indices:		
R	0.036	0.036
R_w	0.040	0.039
GOF	1.107	1.096
Weighting coefficients:	1.73, 1.44, 1.60, 0.35, 0.35	1.13, 0.23, 0.88, –0.04, 0.19
Largest peak/hole (ecm^{-3})	0.29/–0.23	0.24/–0.24

($^3J_{CP}$ = 19.1 Hz, C6), 158.3 ($CO_2CH_2CH_3$),159.4 ($^2J_{CP}$ = 9.4 Hz, C3), 172.3 ($^3J_{CP}$ = 10.0 Hz, C4a).

MS (EI): *m/z* (%) = 382 (49, [M$^+$]), 325 (67), 211 (26, [M$^+$ – 2 $N(CH_2CH_2)_2O$ + H]), 88 (19), 87 (43), 86 (100), 85 (13), 70 (21), 59 (15), 56 (34).

X-ray Crystal Structure Determination of Compounds 27 and 38

Crystal data, data collection, and processing parameters are given in Table 2. All crystallographic measurements were performed at 20 °C on a CAD-4-Enraf-Nonius diffractometer (Mo-K_α radiation, ω-2θ scan mode, ratio of scanning rates ω/2θ = 1.2). All data were corrected for Lorentz and polarization effects and an empirical absorption correction based on azimuthal scan data[13] was applied. The structures were solved by direct methods. Non-hydrogen atoms were refined by full-matrix least-squares technique in the anisotropic approximation. In both structures all hydrogen atoms were located in the difference Fourier maps and included in the final refinement with the fixed positional and thermal parameters. Chebushev weighting scheme[14] was used. All structural calculations were carried out using the CRYSTALS program package.[15]

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