SYNTHESIS AND CHEMICAL REACTIONS OF NEW PHOSPHONO-PHOSPHINO SUBSTITUTED γ-THIAPYRONES

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Dedicated on 75th birthday of Professor Dr. Koji Nakanishi, Columbia-University, with best wishes

Abstract- 1,3-Dithietane-2,4-diylidenebis(cyanomethylphosphonates) and -phenylphosphinates (**1**/**2**) react with various substituted acetonitriles (**3**) to give phosphono-phosphino substituted γ-thiapyrones (**4**/**5**). The constitution of one reaction product is confirmed by an X-ray crystal structure analysis (**4.2 c**). The γ-thiapyrones are converted to boc-protected γ-thiapyrones (**6**/**7**) and to γ-pyrones (**8**/**9**) *via* oxidation.

INTRODUCTION

During the last three decades Organophosphorus Chemistry has become more interest, because some phosphorus containing compounds have been reported to

possess antibiotic, antineoplastic, antiviral or herbicidal attributes,[1] e.g. many pyridazenes and pyrazoles show biological activity[2,3] and aminophosphonic acids have also economic and clinical potential.[4]

In our working group we reported syntheses of new phosphono- and phosphino substituted heterocycles starting *via* simply prepared 1,3-dithietane-2,4-diylidenebis(cyanomethylphosphonates) and -phenylphosphinates.[5a-d]

Peseke and Suarez [6] reported the reaction of 1,3-dithietane-2,4-diylidenebis(cyanoesters) and -cyanoacetamides with benzoylacetonitrile in DMF and potassium carbonate to give the 2-amino-5-cyano-6-phenyl-4-thioxo-4*H*-pyran-3-carbonesters(-carbonamides).

In our investigation it was important to synthesize phosphono-phosphino substituted γ-thiapyrones in order to study the chemical reactivity, spectroscopical data and the biological activity, because there are only some pyrone derivates known as relevant compounds, e.g. chelidonic acid, maltol, meconic acid and kojic acid,[7] but there is no phosphono-phosphino thiapyrone described.

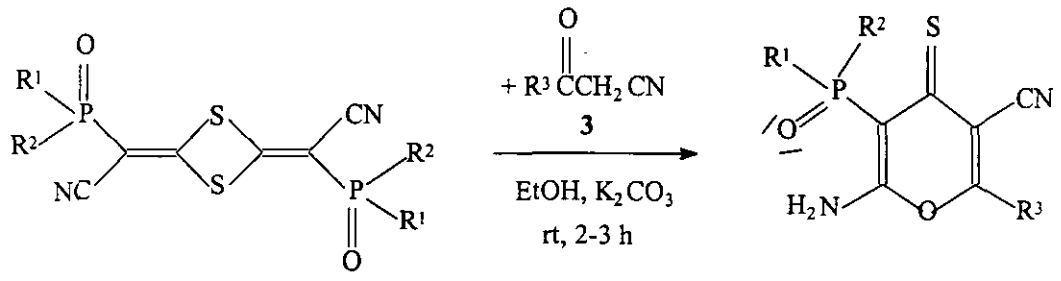
The present paper describes the results of our studies concerning the preparation and reactions of new phosphono-phosphino substituted γ-thiapyrones (**4**/**5**).

RESULTS AND DISCUSSION

The reaction of phosphono- and phosphino substituted 1,3-dithietanes (**1**/**2**) with various substituted acetonitriles (**3**) led to the γ-thiapyrones (**4**/**5**) in a one-stage process (Scheme 1). The starting materials (**1**/**2**) were obtained in moderate yields (10-54 %).[5a]

The structure of the γ-thiapyrones (**4**/**5**) was investigated by NMR spectroscopy (nOe-measurements) and X-ray analysis. The NMR spectra of compound **4.1 b** shows two types of the NH_2-protons [$\delta(H^A)$= 6.55 (br s, 1H) and $\delta(H^B)$= 9.71 (br

s, 1H)].



1/2 4/5

compound	R^1=R^2	R^3
4.1a	OMe	C_6H_5
4.2a	OMe	C_6H_4Cl
4.3a	OMe	tBu
4.4a	OMe	C_6H_4Me
4.5a	OMe	C_4H_3O
4.1b	OEt	C_6H_5
4.2b	OEt	C_6H_4Cl
4.3b	OEt	tBu
4.4b	OEt	C_6H_4Me
4.5b	OEt	C_4H_3O

4.1c	OiPr	C_6H_5
4.2c	OiPr	C_6H_4Cl
4.3c	OiPr	tBu
4.4c	OiPr	C_6H_4Me
4.5c	OiPr	C_4H_3O

compound	R^1, R^2	R^3
5.1d	R^1=OEt R^2=C_6H_5	C_6H_5
5.2d	R^1=OEt R^2=C_6H_5	C_6H_4Cl

Scheme 1: Synthesis of phosphono-phosphino substituted γ-thiapyrones (**4/5**)

The different chemical shifts of the NH_2-protons are the spectroscopic evidence for the presence of intramolecular hydrogen bonds between one of the hydrogens of the NH_2-protons and the oxygen atom of the P=O bonding in the phosphonate group. Besides the nOe-experiment shows us, that the NH_2-protons are localized

at the nitrogen atom of the NH_2-group and there is no imine-enthiol-tautomerism observed in solution (Figure 1).

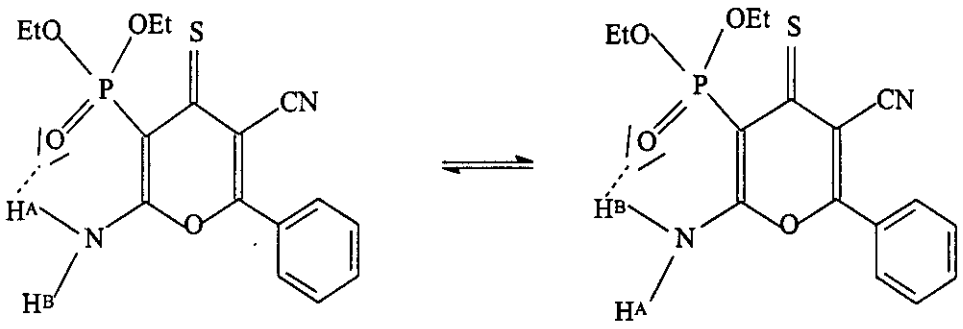


Figure 1: Compound (**4.1 b**) - intramolecular hydrogen bonding -

To obtain further structural information, an X-Ray crystal structure analysis of **4.2 c** was performed (Figure 2)

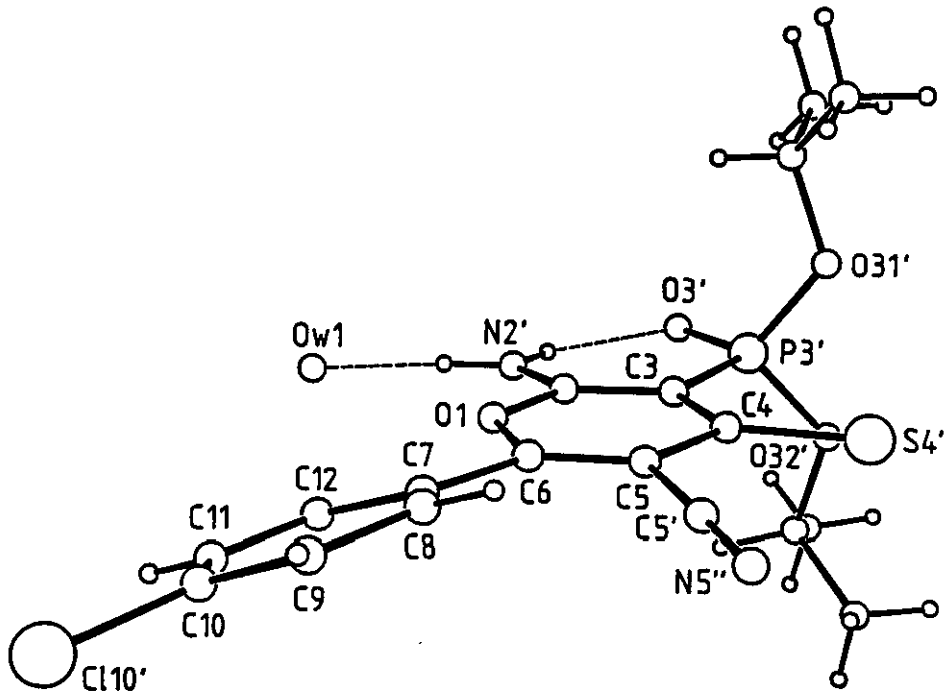


Figure 2: X-Ray structure of compound (**4.2 c**)

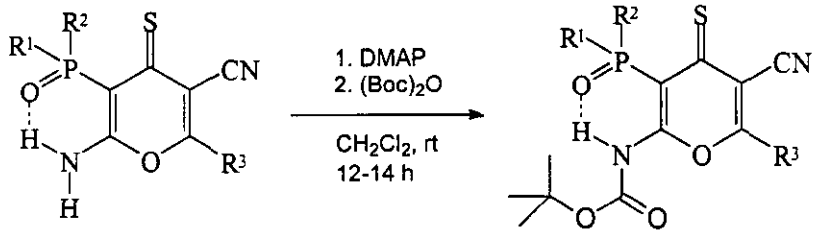
By recrystallisation from chloroform / n-hexane orange monoclinic crystals of **4.2 c** with the space group C 2/c (# 15 Int. Tables) were obtained: $C_{18}H_{20}N_2O_4ClPS*$ 2.5 H_2O, mol. weight= 426.51 $gmol^{-1}$. The unit cell parameters were a= 22.247 (3) Å, b= 9.600 (3) Å, c= 22.272 (3) Å, β= 102.69 (2)°, V= 4640.4 (30) $Å^3$, Z= 8, μ= 3.526 cm^{-1} (Mo K_α), F_{000}= 1976 e. Intesity data were collected using a graphite-monochromated Mo K_α (λ= 0.7107 Å) radiation and applying ω-2Θ-scan technique. Up to sin Θ/λ= 0.62 $Å^{-1}$ 4547 symmetry independent reflections were measured out of which 1966 reflections with $I \geq 3.0$ σ (I) were graded as observed. The structure was solved by the conventional direct method (SIR) and refined by full matrix least squares technique using anisotropic temperature factors for the non-hydrogen atoms and isotropic temperature factors for the hydrogen atoms (R= 0.057, R_w= 0.066). All the atomic coordinates and equivalent isotropic thermal parameters of hydrogen atoms and non-hydrogen atoms are given in Table 1, the bond distances are listed in Table 2, the bond angles are summarized in Table 3 and the torsions angles are given in Table 4.

Figure 2 shows that the molecule is nearly planar with the exception of the isopropoxy groups of the phosphono-substituent in the 3'-position of the γ-thiapyrone and the 4'-chlorophenylligand in the 6'-position. The angel between the neighbouring 4'-chlorophenyl ring and the γ-thiapyrone ring is about 20°. The oxygen-carbon bond lengths of 1.367 (6) Å and 1.368 (6) Å are in accord with other sp^2-carbon-oxygen bond distances reported.[8] The C=S bond length of 1.657 (6) Å is somewhat shorter than that of reported bond lengths.[8] Besides the C5'-N5'bond length of 1.129 (8) Å differs somewhat in that it is shorter than the value described in the literature (1.138 Å).[8] The N2'-O3'distance (2.641 (6) Å shows typical values for N-H···O hydrogen bonds.[9]

The reaction mechanism can be described with an initial nucleophilic attack on

the 1,3-dithietane carbon by the α-C-atom of the substituted acetonitriles. Subsequently cyclization and transformation of the cyanogroup lead directly to the observed γ-thiapyrones (**4/5**).

It was important for us to study the reactivity of the phosphono-γ-thiapyrones (**4/5**). Protecting the amino group of the γ-thiapyrones (**4/5**) with $(Boc)_2O$ in the presence of DMAP as a catalyst led to the 2-*tert*-butoxycarbonylamino γ-thiapyrones (**6/7**) (Scheme 2). This is a well known protecting group in the peptide chemistry.[10,11]



4/5 **6/7**

compound	R^1=R^2	R^3
6.2a	OMe	C_6H_4Cl
6.3a	OMe	tBu
6.1b	OEt	C_6H_5
6.2b	OEt	C_6H_4Cl
6.2c	OiPr	C_6H_4Cl
6.4c	OiPr	C_6H_4Me

compound	R^1, R^2	R^3
7.1d	R^1=OEt R^2=Ph	C_6H_5
7.2d	R^1=OEt R^2=Ph	C_6H_4Cl

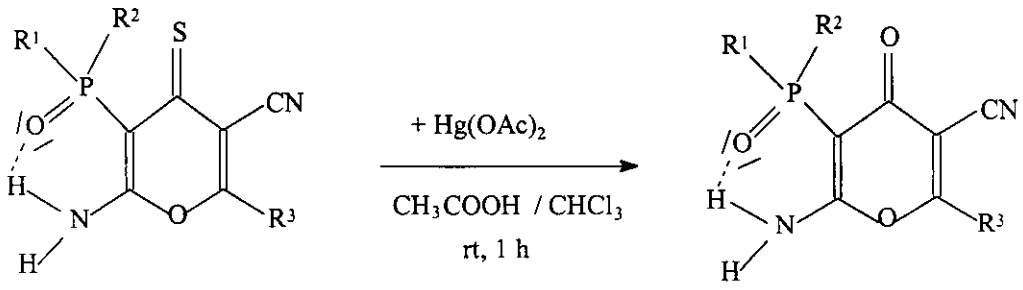
Scheme 2: Synthesis of 2-*tert*-butoxycarbonylamino γ-thiapyrones (**6/7**)

The ^1H NMR spectra of the compounds (**6/7**) show a sharp singulet of the NH-

proton at 12.00-12.20 ppm. It could be explained as the hydrogen-bonding of the NH-proton to the oxygen atom of the P=O bonding in the phosphonate (-phosphinate) group. The signal of the NH-proton is more downfield shifted as it is located in the free γ-thiapyrones (**4/5**). The CS-carbon signal in the ^{13}C NMR spectra is observed by 192-194 ppm and the quaterny carbon atom of the CN-group is at about 114 ppm.[12] The C-3 atom in the ^{13}C NMR is given as a doublet at about 100 ppm ($^{1}J_{CP} \approx$ 195 Hz).

In the IR spectra the CN-group is located at 2229-2233 cm^{-1} as a weak band and the ester-function at 1755-1760 cm^{-1} as a strong sharp band.[13]

Besides it was important for us to have a simple route in order to oxidize the γ-thiapyrones (**4/5**) to give the phosphono-phosphino substituted γ-pyrones (**8/9**). There are some methods known in the literature to transform the thia carbonyl to the carbonyl group. The best known method is to oxidize the compound with $Hg(OAc)_2$ in glacial acidic acid and chloroform at rt.[14a,b] The oxidation of the γ-thiapyrones (**4/5**) with $Hg(OAc)_2$ led to the phosphono-phosphino substituted γ-pyrones (**8/9**) (Scheme 3).



4/5 **8/9**

compound	$R^1=R^2$	R^3
8.4a	OMe	C_6H_4Me

8.2b	OEt	C_6H_4Cl
8.1c	OiPr	C_6H_5
compound	R^1, R^2	R^3
9.2d	R^1=OEt R^2=Ph	C_6H_4Cl

Scheme 3: Synthesis of γ-pyrones (**8/9**)

The compounds (**8/9**) are given in the IR spectra a sharp strong band at about 1650 cm^{-1}. The absorption band of the carbonyl group is very characteristic for cyclic-enone-systems as it is described in the literature.[13] The CN group is located at 2225-2230 cm^{-1} as a weak band in the IR spectra. There are still two types of NH_2-protons [$\delta(H^A) \approx$ 6.10 ppm (br s, 1H) and $\delta(H^B) \approx$ 9.00 ppm (br s, 1H)]. These NH_2-protons of the γ-pyrones (**8/9**) are a little bit highfield shifted as in the γ-thiapyrones (**4/5**). The CO carbon signal in the ^{13}C-NMR spectra is observed by 170-172 ppm and the quaterny carbon atom of the CN group at about 112 ppm.[12] The C-3 atom is given a doublet at about 85 ppm ($^1J_{CP} \approx$ 195 Hz). The UV spectra of the γ-pyrones (**8/9**) are characterized by an intense absorption band at 245-250 nm. It is in agreement with some typical examples known in the literature.[15] The absorption band of the γ-thiapyrones (**4/5**) are somewhat higher (λ_{max}= 255-265 nm).

EXPERIMENTAL

Melting points were determined on a Reichert hot stage microscope and are uncorrected. IR spectra were measured with a Perkin-Elmer IR

spectrophotometer 1600 (FT IR) and are given in cm^{-1}. ^1H- and ^{13}C-NMR spectra were recorded on either a Bruker WM-250 (^1H-NMR: 250.13 MHz, ^{13}C-NMR: 62.89 MHz), Bruker WM-360 (^1H-NMR: 360 MHz, ^{13}C-NMR: 90.56 MHz) or a Varian XL 300 (^1H-NMR: 299.95 MHz, ^{13}C-NMR: 75.43 MHz) spectrometer in $CDCl_3$. All chemical shifts are reported in ppm downfield from tetramethylsilane; coupling constants J are given in Hz. ^{31}P-NMR spectra were measured with Varian XL 300 (^{31}P-NMR: 121.42 MHz) and Bruker WM-360 (^{31}P-NMR: 145.79 MHz) spectrometer using H_3PO_4 (internal standard 85 % H_3PO_4). EIMS were recorded on a Varian MAT 311 A spectrometer (70 eV). UV spectra were measured with a Hewlett Packard 8452 A Diode Array spectrometer in acetonitrile. Element analyses were performed on a Heraus Vario EL CHNS apparatus.

General procedure for the preparation of phosphono-phosphino substituted γ-thiapyrones (**4**/**5**)

To a solution of 1 mmol phosphono-phosphino substituted dithietanes (**1**/**2**) in EtOH (15 mL), K_2CO_3 (207 mg, 1.5 mmol) were added substituted acetonitriles (**3**) (2 mmol). The reaction mixture was stirred for 2-3 h at rt. Water was added (10 mL) and the solution was acidified with concentrated hydrogen chloride (5 mL). The resulting solution was extracted with chloroform (3*20 mL). The combined organic layers were dried over anhydrous $MgSO_4$. After evaporation of the solvent, the red oil was chromatographed on silica gel (ethyl acetate / n-hexane (1:1) to give the γ-thiapyrones (**4**/**5**) as orange crystals.

2-Amino-5-cyano-6-phenyl-4-thioxo-4*H*-pyran-3-ylphosphonic acid dimethyl ester

(**4.1a**)

-160 mg (48 %) **4.1a** were obtained after chromatographic separation as orange crystals, mp 163 - 164 °C. ^{1}H-NMR (300 MHz, $CDCl_3$) δ= 3.80, 3.84 (d_p, $^3J_{HP}$= 12 Hz, 6H, OC$\underline{H}_3$), 5.89 (br s, 1H, NH^a, NH_2), 7.52 - 8.03 (m, 5H, 2'-H, 3'-H, 4'-H, 5'-H, 6'-H), 9.75 (br s, 1H, NH^b, NH_2). ^{13}C-NMR (62.89 MHz, $CDCl_3$) δ= 53.6 (d_p, $^2J_{CP}$= 6.2 Hz, O$\underline{C}H_3$), 97.4 (d_p, $^1J_{CP}$= 200 Hz, C-3), 108.1 (d_p, $^3J_{CP}$= 11.9 Hz, C-5), 114.5 (s, CN), 128.3 (s, C-1'), 128.6, 129.2 (2*d, C-2', C3', C-5', C-6'), 133.2 (s, C-4'), 156.8 (s, C-6), 163.1 (d_p, $^2J_{CP}$= 26.1Hz, C-2), 193.0 (d_p, $^2J_{CP}$= 7.5Hz, CS). ^{31}P-NMR (121.42 Mhz, $CDCl_3$) δ= 20.9 (s). IR (KBr, tablet) ν= 3342 (m), 3283 (m), 3060 (w), 2927 (w), 2224 (w), 1617 (s) 1598 (w), 1542 (w), 1506 (s), 1498 (w), 1467 (w), 1457 (w), 1445 (w), 1373 (s), 1315 (w), 1298 (w), 1270 (m), 1233(m), 1191 (w), 1169 (w), 1102 (w), 1029 (br s), 1000 (w), 884 (m), 841 (m), 804 (m), 772 (w), 737 (w), 696 (w), 668 (w), 645 (w), 567 (w), 503 (w), 419 (w), 405 (w). MS (70 eV, 167 °C) m/z (%)= 336 (M^+, 9), 105 ($C_6H_5CO^+$, 60), 77 ($C_6H_5^+$, 100), 51 ($C_4H_3^+$, 18). UV (MeCN) λ_{max} (log ε)= 251 (4.19), 298 (4.41), 322 (3.85, sh), 366 (3.61, sh). Exact mass calcd for $C_{14}H_{13}N_2O_4PS$: 336.3111. Found: 336.3110.

2-Amino-5-cyano-6-(4'-chlorophenyl)-4-thioxo-4*H*-pyran-3-ylphosphonic acid dimethyl ester (**4.2a**)

-190 mg (51 %) **4.2a** were obtained as orange crystals after chromatographic separation, mp 155-156 °C. ^{1}H-NMR (300 MHz, $CDCl_3$) δ= 3.79, 3.83 (d_p, $^3J_{HP}$= 12 Hz, 6H, OC$\underline{H}_3$), 6.44 (br s, 1H, NH^a, NH_2), 7.49-7.52 (d, $^3J_{HH}$= 8.7 Hz, 2H, 3'-

H, 5'-H), 7.94-7.97 (d, $^3J_{HH}$= 8.7 Hz, 2H, 2'-H, 6'-H), 9.68 (br s, 1H, NH^b, NH_2). ^{13}C-NMR (75.43 MHz, $CDCl_3$) δ= 53.7 (d_p, $^2J_{CP}$= 6.4 Hz, O<u>C</u>H$_3$) 97.5 (d_p, $^1J_{CP}$= 199 Hz, C-3), 108.4 (d_p, $^3J_{CP}$= 12 Hz, C-5), 114.2 (s, CN), 126.7 (s, C-1'), 129.5, 129.9 (2*d, C-2', C-3', C-5', C-6'), 139.8 (s, C-4'), 158.7 (s, C-6), 162.6 (d_p, $^2J_{CP}$= 26.5 Hz), 193.6 (d_p, $^2J_{CP}$= 8 Hz, CS). ^{31}P-NMR (121.42 MHz, $CDCl_3$) δ= 20.6 (s). IR (KBr, tablet) ν= 3451 (w), 3233 (w), 3051 (w), 2983 (w), 2879 (w), 2222 (w), 1635 (s), 1603 (s), 1592 (m), 1559 (w), 1539 (w), 1521 (w), 1506 (w), 1490 (w), 1457 (w), 1403 (m), 1377 (s), 1283 (m), 1265 (w), 1242 (w), 1187 (w), 1163 (w), 1091 (w), 1037 (s), 1014 (w), 981 (w), 884 (w), 846 (w), 835 (w), 821 (w), 803 (w), 741 (w), 668 (w), 586 (w), 491 (w), 408 (w), 402 (w). MS (70 eV, 167 °C) m/z (%)= 370 (M^+, 6), 139 ($ClC_6H_4CO^+$, 85), 111 ($ClC_6H_4^+$, 100), 75 ($C_6H_3^+$, 44). UV (MeCN) λ_{max} (log ε)= 253 (4.15), 300 (4.42), 324 (3.84, sh), 375 (3.62, sh). Anal. Calcd for $C_{14}H_{12}N_2O_4ClPS$: C, 45.34; H, 3.26; N, 7.58; S, 8.64. Found: C, 45.43; H, 3.46; N, 7.37; S, 8.39.

<u>2-Amino-5-cyano-6-*tert*-butyl-4-thioxo-4*H*-pyran-3-ylphosphonic acid dimethyl ester (**4.3a**)</u>

-140 mg (44 %) **4.3a** were obtained as yellow-orange crystals after chromatographic separation, mp 161-162°C. ^{1}H-NMR (*300 MHz, CDCl$_3$*) δ= *1.50* (s, 9H, C(C<u>H</u>$_3$)$_3$), 3.77, 3.81 (d_p, $^3J_{HP}$= 12 Hz, 6H, OC<u>H</u>$_3$), 5.84 (br s, 1H, NH^a, NH_2), 9.58 (br, s, 1H, NH^b, NH_2). ^{13}C-NMR (75.43 MHz, $CDCl_3$) δ= 27.5 (s, C(<u>C</u>H$_3$)$_3$), 37.3 (s, (CH$_3$)$_3$<u>C</u>), 53.1 (d_p, $^2J_{CP}$= 6.5 Hz, O<u>C</u>H$_3$), 95.6 (d_p, $^1J_{CP}$= 201 Hz, C-3), 108.1 (d_p, $^3J_{CP}$= 11.8 Hz, C-5), 113.3 (s, CN), 162.0 (d_p, $^2J_{CP}$= 26.3 Hz, C-2), 170.4 (s, C-4), 193.2 (d_p, $^2J_{CP}$= 7.6 Hz, CS). ^{31}P-NMR (121.42 MHz, $CDCl_3$)

δ= 20.8 (s). IR (KBr, tablet) ν= 3371 (w), 3160 (w), 3020 (w), 2990 (w), 2872 (w), 2223 (w), 1616 (s), 1601 (w), 1581 (m), 1559 (w), 1539 (w), 1521 (w), 1506 (w), 1480 (w), 1457 (w), 1421 (w), 1400 (w), 1394 (w), 1361 (w), 1262 (m), 1227 (w), 1131 (m), 1090 (w), 1022 (br s), 998 (w), 905 (w), 823 (w), 791 (w), 750 (w), 712 (w), 668 (w), 612 (w), 591 (w), 525 (w), 487 (w), 429 (w), 410 (w), 403 (w). MS (70 eV, 162°C) m/z (%)= 316 (M^+, 68), 109 ($C_2H_6O_3P^+$, 64), 57 ($C_4H_9^+$, 100), 41 ($C_3H_5^+$, 90). UV (MeCN) λ_{max} (log ε)= 238 (4.38), 281 (4.25), 325 (3.85, sh), 344 (3.58, sh). Exact mass calcd for $C_{12}H_{17}N_2O_4PS$: 316.0647. Found: 316.0647.

2-Amino-5-cyano-6-*p*-tolyl-4-thioxo-4*H*-pyran-3-ylphosphonic acid dimethyl ester (**4.4a**)

-220 mg (63 %) **4.4a** were obtained as orange crystals after chromatographic separation, mp 154-155°C. ^{1}H-NMR (300 MHz, $CDCl_3$) δ= 2.44 (s, 3H, $C_6H_4C\underline{H}_3$), 3.80, 3.84 (d_p, $^3J_{HP}$= 11.8 Hz, 6H, $OC\underline{H}_3$), 5.87 (br s, 1H, NH^a, NH_2), 7.33-7.36 (d, $^3J_{HH}$= 8.4 Hz, 2H, 3'-H, 5'-H), 7.87-7.90 (d, $^3J_{HH}$= 8.4 Hz, 2H, 2'-H, 6'-H), 9.71 (br s, 1H, NH^b, NH_2). ^{13}C-NMR (75.43 MHz, $CDCl_3$)δ= 21.5 (s, $C_6H_4\underline{C}H_3$), 53.2 (d_p, $^2J_{CP}$= 6.4 Hz, $O\underline{C}H_3$), 95.7 (d_p, $^1J_{CP}$= 199 Hz, C-3), 108.2 (d_p, $^3J_{CP}$= 11.9 Hz, C-5), 113.5 (s, CN), 125.7 (s, C-1'), 128.8, 129.4 (2*d, C-2', C-3', C-5', C-6'), 139.3 (s, C-4'), 161.9 (d_p, $^2J_{CP}$= 26.5 Hz, C-2), 169.8 (s, C-6), 193.4 (d_p, $^2J_{CP}$= 7.5 Hz, CS). ^{31}P-NMR (145.79 MHz, $CDCl_3$) δ= 20.6 (s). IR (KBr, tablet) ν= 3392 (w), 3101 (w), 2986 (w), 2826 (w), 2225 (w), 1635 (s), 1623 (w), 1617 (w), 1576 (m), 1569 (w), 1533 (w), 1521 (w), 1507 (w), 1498 (w), 1472 (w), 1465 (w), 1457 (w), 1436 (w), 1419 (w), 1387 (w), 1291 (w), 1270 (m),

1217 (w), 1146 (w), 1033 (br s), 882 (m), 836 (w), 821 (w), 772 (w), 739 (w), 668 (w), 607 (m), 524 (w), 484 (w), 463 (w), 413 (w), 406 (w). MS (70 eV, 165°C) m/z (%)= 350 (M^+, 35), 119 ($C_8H_7O^+$, 96), 109 ($C_2H_6O_3P^+$, 18), 91 ($C_7H_7^+$, 100), 65 ($C_5H_5^+$, 34). UV (MeCN) λ_{max} (log ε)= 255 (4.21), 302 (4.45), 322 (3.83, sh), 368 (3.59, sh). Exact mass calcd for $C_{15}H_{15}N_2O_4PS$: 350.0911. Found: 350.0910.

2-Amino-5-cyano-6-furoyl-4-thioxo-4*H*-pyran-3-ylphosphonic acid dimethyl ester (**4.5a**)

-180 mg (55 %) **4.5a** were obtained as orange crystals after chromatographic separation, mp 144-145°C. ^{1}H-NMR (300 MHz, $CDCl_3$) δ= 3.71, 3.75 (d_p, $^3J_{HP}$= 12 Hz, 6H, OC$\underline{H}_3$), 6.25 (br s, 1H, NH^a, NH_2), 6.63 (d, $^3J_{HH}$= 3.9 Hz, 1H, 5'-H), 7.61.7.72 (2*d, $^3J_{HH}$= 3.9 Hz, 2H, 3'-H, 4'-H), 9.63 (br s, 1H, NH^b, NH_2). ^{13}C-NMR (90.56 MHz, $CDCl_3$) δ= 53.6 (d_p, $^2J_{CP}$= 5.8 Hz, O$\underline{C}H_3$), 95.6 (d_p, $^1J_{CP}$= 202 Hz, C-3), 103.5 (d_p, $^3J_{CP}$= 12.2 Hz, C-5), 113.7 (s, C-3') 114.0 (s, CN), 120.3 (s, C-4'), 142.3 (s, C-2'), 148.1 (s, C-5'), 148.8 (s, C-6), 162.5 (d_p, $^2J_{CP}$= 26.5 Hz, C-2), 192.6 (d_p, $^2J_{CP}$= 7.3 Hz, CS). ^{31}P-NMR (121.42 MHz, $CDCl_3$) δ= 20.9 (s). IR (KBr, tablet) ν= 3447 (w), 3266 (w), 3126 (w), 3058 (w), 2961 (w), 2227 (w), 1635 (s), 1617 (w), 1576 (m), 1559 (m), 1539 (w), 1521 (w), 1507 (w), 1499 (w), 1472 (w), 1457 (w), 1437 (w), 1405 (w), 1369 (w), 1285 (w), 1253 (m), 1194 (w), 1121 (w), 1026 (br s), 986 (w), 935 (w), 886 (w), 847 (w), 822 (w), 787 (w), 737 (w), 668 (w), 599 (w), 586 (w), 516 (w), 498 (w), 485 (w), 448 (w), 435 (w), 418 (w), 409 (w), 401 (w). MS (70 eV, 167°C) m/z (%)= 326 (M^+, 26), 109 ($C_2H_6O_3P^+$, 38), 95 ($C_5H_3O_2^+$, 100). UV (MeCN) λ_{max} (log ε)= 257 (4.22), 304

(4.45), 324 (3.85, sh), 370 (3.62, sh). Anal. Calcd for $C_{12}H_{11}N_2O_5PS$: C, 44.16; H, 3.39; N, 8.61; S, 9.82. Found: C, 43.87; H, 3.65; N, 8.39; S, 9.99.

2-Amino-5-cyano-6-phenyl-4-thioxo-4*H*-pyran-3-ylphosphonic acid diethyl ester (**4.1b**)

-260 mg (71 %) **4.1b** as orange crystals were obtained after chromatographic separation, mp 138°C. ^{1}H-NMR (300 MHz, $CDCl_3$) δ= 1.34 (d_pt, $^3J_{HH}$= 6.9 Hz, 6H, OCH_2CH_3), 4.06-4.21 (m, 4H, OCH_2CH_3), 6.55 (br s, 1H, NH^a, NH_2), 7.49-7.63 (m, 3H, 3'-H, 4'-H, 5'-H), 7.97-7.99 (m, 2H, 2'-H, 6'-H), 9.71 (br s, 1H, NH^b, NH_2). ^{13}C-NMR (62.89 MHz, $CDCl_3$) δ= 16.2 (d_p, $^3J_{CP}$= 7.5 Hz, OCH_2CH_3), 63.5 (d_p, $^2J_{CP}$= 5.2 Hz, OCH_2CH_3), 97.2 (d_p, $^1J_{CP}$= 200 Hz, C-3), 108.2 (d_p, $^3J_{CP}$= 12.2 Hz, C-5), 114.8 (s, CN), 128.4 (s, C-1'), 128.6, 129.1 (2*d, C-2', C-3', C-5', C-6'), 133.2 (s, C-4'), 159.0 (s, C-6), 163.0 (d_p, $^2J_{CP}$= 25.9 Hz, C-2), 193.3 (d_p, $^2J_{CP}$= 7.6 Hz, CS). ^{31}P-NMR (121.42 MHz, $CDCl_3$) δ= 16.7 (s). IR (KBr, tablet) ν= 3273 (w), 3127 (w), 2983 (w), 2228 (w), 1629 (s), 1602 (w), 1571 (m), 1536 (w), 1507 (w), 1496 (w), 1437 (w), 1446 (w), 1376 (s), 1267 (s), 1236 (m), 1163 (m), 1127 (w), 1055 (m), 1025 (br s), 976 (m), 880 (s), 774 (m), 737 (m), 693 (m), 647 (m), 603 (w), 591 (w), 565 (w), 511 (w), 489 (w), 469 (w), 440 (w), 422 (w), 411 (w), 403 (w). MS (70 eV, 178°C) m/z (%)= 365 (7), 364 (M^+, 28), 105 ($C_6H_5CO^+$, 100), 77 ($C_6H_5^+$, 87), 51 ($C_4H_3^+$, 5). UV (MeCN) λ_{max} (log ε)= 252 (4.18), 298 (4.43), 320 (3.89, sh), 362 (3.61, sh). Exact mass calcd for $C_{16}H_{17}N_2O_4PS$: 364.0647. Found: 364.0645.

2-Amino-5-cyano-6-(4'-chlorophenyl)-4-thioxo-4*H*-pyran-3-ylphosphonic acid

diethyl ester (**4.2b**)

-230 mg (58 %) **4.2b** were obtained as orange-red crystals after chromatographic separation, mp 157°C. ^{1}H-NMR (300 MHz, $CDCl_3$) δ= 1.36 (d_pt, $^3J_{HH}$= 6.9 Hz, 6H, OCH_2CH_3), 4.08-4.28 (m, 4H, OCH_2CH_3), 5.95 (br s, 1H, NH^a, NH_2), 7.51-7.55 (d, $^3J_{HH}$= 8.1 Hz, 2H, 3'-H, 5'-H), 7.94-7.97 (d, $^3J_{HH}$= 8.1 Hz, 2H, 2'-H, 6'-H), 9.84 (br s, 1H, NH^b, NH_2). ^{13}C-NMR (75.43 MHz, $CDCl_3$) δ= 16.2 (d_p, $^3J_{CP}$= 7.2 Hz, OCH_2CH_3) 63.4 (d_pt, $^2J_{CP}$= 5.5 Hz, OCH_2CH_3), 97.5 (d_p, $^1J_{CP}$= 198 Hz, C-3), 108.2 (d_p, $^3J_{CP}$= 11.8 Hz, C-5), 114.5 (s, CN), 126.6 (s, C-1'), 129.3, 129.9 (2*d, C-2', C-3', C-5', C-6'), 139.5 (d, C-4'), 157.5 (s, C-6), 162.6 (d, $^2J_{CP}$= 26.2 Hz, C-2), 192.6 (d_p, $^2J_{CP}$= 7.2 Hz, CS). ^{31}P-NMR (121.42 MHz, $CDCl_3$) δ= 16.2 (s). IR (KBr, tablet) ν= 3395 (w), 3128 (w), 2978 (w), 2227 (w), 1635 (s), 1559 (s), 1539 (m), 1507 (m), 1490 (w), 1457 (w), 1437 (m), 1404 (m), 1374 (s), 1283 (m), 1263 (s), 1163 (m), 1092 (m), 1023 (br s), 978 (m), 880 (m), 799 (w), 743 (w), 668 (w), 603 (w), 561 (m), 513 (w), 485 (w), 413 (w), 402 (w). MS (70 eV, 178°C) m/z (%)= 399 (29), 398 (M^+, 53), 139 ($ClC_6H_4CO^+$, 100), 111 ($ClC_6H_4^+$, 30), 75 ($C_6H_3^+$, 18). UV (MeCN) λ_{max} (log ε)= 254 (4.22), 301 (4.45), 322 (3.90, sh), 370 (3.60, sh). Exact mass calcd for $C_{16}H_{16}N_2O_4ClPS$: 398.0259. Found: 398.0258.

2-Amino-5-cyano-6-*tert*-butyl-4-thioxo-4*H*-pyran-3-ylphosphonic acid diethyl ester (**4.3b**)

-160 mg (47 %) **4.3b** were obtained as yellow-orange crystals after chromatographic separation, mp 102°C. ^{1}H-NMR (300 MHz, $CDCl_3$) δ= 1.35 (d_pt,

$^3J_{HH}$= 7.2 Hz, 6H, $OCH_2C\underline{H}_3$), 1.51 (s, 9H, $(C\underline{H}_3)_3C$), 4.06-4.25 (m, 4H, $OC\underline{H}_2CH_3$), 6.46 (br s, 1H, NH^a, NH_2), 9.60 (br s, 1H, NH^b, NH_2). ^{13}C-NMR (75.43 MHz, $CDCl_3$) δ= 16.2 (d_p, $^3J_{CP}$= 6.9 Hz, $OCH_2\underline{C}H_3$), 27.9 (s, $(\underline{C}H_3)_3C$), 37.5 (s, $(CH_3)_3\underline{C}$), 63.3 (d_p, $^2J_{CP}$= 5.6 Hz, $O\underline{C}H_2CH_3$), 96.7 (d_p, $^1J_{CP}$= 200 Hz, C-3), 108.5 (d_p, $^3J_{CP}$= 12 Hz, C-5), 114.0 (s, CN), 162.2 (d_p, $^2J_{CP}$= 21 Hz, C-2), 171.5 (s, C-6), 193.4 (d_p, $^2J_{CP}$= 7.8 Hz, CS). ^{31}P-NMR (121.42 MHz, $CDCl_3$) δ= 16.5 (s). IR (KBr, tablet) ν= 3244 (w), 3125 (w), 2980 (w), 2228 (w), 1628 (s), 1600 (w), 1585 (w), 1560 (w), 1540 (w), 1517 (w), 1495 (w), 1471 (w), 1451 (w), 1396 (w), 1364 (s), 1271 (s), 1232 (m), 1188 (m), 1099 (w), 1014 (br s), 981 (m), 910 (m), 779 (w), 670 (w), 615 (w), 543 (w), 448 (w), 430 (w), 405 (w). MS (70 eV, 123°C) m/z (%)= 345 (14), 344 (M^+, 80), 109 ($C_2H_6O_3P^+$, 73), 81 ($H_2O_3P^+$, 68), 57 ($C_4H_9^+$, 100). UV (MeCN) λ_{max} (log ε)= 237 (4.46), 281 (4.25), 323 (3.72). Exact mass calcd for $C_{14}H_{21}N_2O_4PS$: 344.0959. Found: 344.0958.

2-Amino-5-cyano-6-*p*-tolyl-4-thioxo-4*H*-pyran-3-ylphosphonic acid diethyl ester (**4.4b**)

-220 mg (58 %) **4.4b** were obtained as orange-red crystals after chromatographic separation, mp 130°C. ^{1}H-NMR (300 MHz, $CDCl_3$) δ= 1.34 (d_pt, $^3J_{HH}$= 6.9 Hz, 6H, $OCH_2C\underline{H}_3$), 2.43 (s, 3H, $C_6H_4C\underline{H}_3$), 4.08-4.22 (m, 4H, $OC\underline{H}_2CH_3$), 6.17 (br s, 1H, NH^a, NH_2), 7.31-7.34 (d, $^3J_{HH}$= 8.1 Hz, 2H, 3'-H, 5'-H), 7.87-7.90 (d, $^3J_{HH}$= 8.1 Hz, 2H, 2'-H, 6'-H), 9.74 (br s, 1H, NH^b, NH_2). ^{13}C-NMR (90.56 MHz, $CDCl_3$) δ= 16.2 (d_pq, $^3J_{CP}$= 7 Hz, $OCH_2\underline{C}H_3$), 21.7 (s, $C_6H_4\underline{C}H_3$), 63.5 (d_pt, $^2J_{CP}$= 5 Hz, $O\underline{C}H_2CH_3$), 97.1 (d_p, $^1J_{CP}$= 200 Hz, C-3), 107.8 (d_p, $^2J_{CP}$= 12.4 Hz, C-5),

114.9 (s, CN), 125.4 (s, C-1'), 128.6, 129.8 (2*d, C-2', C-3', C-5', C-6'), 144.4 (s, C-4'), 159 .1 (s, C-6), 163.0 (d_p, $^2J_{CP}$= 26.3 Hz, C-2), 193.1 (d_p, $^2J_{CP}$= 7.9 Hz, CS). ^{31}P-NMR (121.42 MHz, $CDCl_3$) δ= 17.3 (s). IR (KBr, tablet) ν= 3463 (w), 3255 (w), 3085 (w), 2990 (w), 2976 (w), 2225 (w), 1628 (s), 1605 (w), 1559 (m), 1540 (w), 1507 (w), 1496 (w), 1457 (w), 1437 (w), 1377 (s), 1267 (s), 1239 (m), 1164 (m), 1029 (br s), 978 (w), 883 (w), 823 (w), 741 (w), 607 (w), 567 (w), 501 (w), 448 (w), 440 (w), 419 (w), 411 (w), 405 (w). MS (70 eV, 193°C) m/z (%)= 379 (9), 378 (M^+, 39), 119 ($C_8H_7O^+$, 100), 91 ($C_7H_7^+$, 85), 65 ($C_5H_5^+$, 26). UV (MeCN) λ_{max} (log ε)= 256 (4.21), 302 (4.42), 322 (3.84, sh), 368 (3.59, sh). Anal. Calcd for $C_{17}H_{19}N_2O_4PS$: C, 53.96; H, 5.06; N, 7.40; S, 8.47. Found: C, 53.77; H, 5.06; N, 7.41; S, 8.75.

2-Amino-5-cyano-6-furoyl-4-thioxo-4*H*-pyran-3-ylphosphonic acid diethyl ester (**4.5b**)

-200 mg (57%) **4.5b** were obtained as orange-red crystals after chromatographic separation, mp 151-152°C. ^{1}H-NMR (300 MHz, $CDCl_3$) δ= 1.34 (d_pt, $^3J_{HH}$= 6.2 Hz, 6H, $OCH_2\underline{C}H_3$), 4.05-4.27 (m, 4H, $O\underline{C}H_2CH_3$), 6.24 (br s, 1H, NH^a, NH_2), 6.71 (d, $^3J_{HH}$= 3.9 Hz, 1H, 5'-H), 7.68, 7.80 (2*d, $^3J_{HH}$= 3.9 Hz, 3'-H, 4'-H), 9.70 (br s, 1H, NH^b, NH_2). ^{13}C-NMR (62.89 MHz, $CDCl_3$) δ= 16.2 (d_p, $^3J_{CP}$= 7.2 Hz, $OCH_2\underline{C}H_3$), 63.4 (d_p, $^2J_{CP}$= 5.5 Hz, $O\underline{C}H_2CH_3$), 96.4 (d_p, $^1J_{CP}$= 201 Hz, C-3), 103.2 (d_p, $^3J_{CP}$= 12.4 Hz, C-5), 113.7 (s, C-3'), 114.1 (s, CN), 120.3 (s, C-4'), 142.4 (s, C-2'), 148.1 (s, C-5'), 148.8 (s, C-6), 162.4 (d_p, $^2J_{CP}$= 26.6 Hz, C-2), 192.8 (d_p, $^2J_{CP}$= 7.6 Hz, CS). ^{31}P-NMR (1121.42 MHz, $CDCl_3$) δ= 16.7 (s). IR (KBr, tablet) ν= 3240 (w), 3098 (w), 2980 (w), 2231 (w), 1628 (s), 1601 (w), 1559

(m), 1539 (w), 1506 (w), 1472 (w), 1437 (w), 1395 (w), 1371 (w), 1287 m), 1244 (s), 1188 (m), 1125 (w), 1026 (br s), 979 (m), 921 (w), 884 (w), 852 (w), 800 (w), 755 (w), 668 (w), 589 (w), 492 (w), 446 (w), 427 (w), 408 (w), 402 (w). MS (70 eV, 173°C) m/z (%)= 355 (9), 354 (M^+, 45), 95 ($C_5H_3O_2^+$, 100), 67 ($C_4H_3O^+$, 30). UV (MeCN) λ_{max} (log ε)= 265 (4.20), 309 (4.44), 352 (3.85), 401 (3.58). Anal. Calcd for $C_{14}H_{15}N_2O_5PS$: C, 47.45; H, 4.27; N, 7.90; S, 9.04. Found: C, 47.20; H, 4.48; N, 7.74; S, 9.18.

2-Amino-5-cyano-6-phenyl-4-thioxo-4*H*-pyran-3-ylphosphonic acid diisopropyl ester (**4.1c**)

-290 mg (73%) **4.1c** were obtained as orange-red crystals after chromatographic separation, mp 81°C. ^{1}H-NMR (300 MHz, $CDCl_3$) δ= 1.32, 1.37 (2*d_p, $^3J_{HH}$= 6.3 Hz, 12H, OCH($C\underline{H}_3$)$_2$), 4.64-4.75 ($d_p$sept, $^2J_{HP}$= 7.5 Hz, 2H, OC$\underline{H}$(CH_3)$_2$), 6.28 (br s, 1H, NH^a, NH_2), 7.49-7.63 (m, 3H, 3'-H, 4'-H, 5'-H), 7.95-7.99 (m, 2H, 2'-H, 6'-H), 9.84 (br s, 1H, NH^b, NH_2). ^{13}C-NMR (75.43 MHz, $CDCl_3$) δ= [23.8 (d_p, $^3J_{CP}$= 6 Hz), 24.0 (d_p, $^3J_{CP}$= 5 Hz, OCH($\underline{C}H_3$)$_2$], 72.8 (d_pd, $^2J_{CP}$= 5 Hz, O$\underline{C}$H(CH_3)$_2$), 98.2 (d_p, $^1J_{CP}$= 196 Hz, C-3), 108.3 (d_p, $^3J_{CP}$= 11.3 Hz, C-5), 114.7 (s, CN), 128.3 (s, C-1'), 128.4, 128.9 (2*d, C-2', C-3', C-5', C-6'), 132.9 (s, C-4'), 158.5 (s, C-6), 162.5 (d_p, $^2J_{CP}$= 24.2 Hz, C-2), 192.8 (d_p, $^2J_{CP}$= 7.2 Hz, CS). ^{31}P-NMR (121.42 MHz, $CDCl_3$) δ= 13.4 (s). IR (KBr, tablet) ν= 3496 (w), 3202 (w), 3106 (w), 2978 (w), 2932 (w), 2226 (w), 1628 (s), 1593 (s), 1569 (m), 1506 (m), 1465 (w), 1445 (w), 1371 (s), 1265 (s), 1227 (w), 1172 (m), 1142 (m), 1104 (m), 1013 (br s), 972 (m), 937 (w), 893 (w), 784 (w), 737 (m), 694 (m), 648 (m), 579 (w), 463 (w), 420 (w), 406 (w). MS (70 eV, 197°C) m/z (%)= 393 (6), 392

(M^+, 25), 349 (M^+ - $C_3H_7^+$, 34), 105 ($C_6H_5CO^+$, 100), 77 ($C_6H_5^+$, 28), 51 ($C_4H_3^+$, 11). UV (MeCN) λ_{max} (log ε)= 259 (4.16), 298 (4.41), 321 (3.87, sh), 366 (3.58, sh). Exact mass calcd for $C_{18}H_{21}N_2O_4PS$: 392. 0960. Found: 392.0960.

2-Amino-5-cyano-6-(4'-chlorophenyl)-4-thioxo-4*H*-pyran-3-ylphosphonic acid di-isopropyl ester (**4.2c**)

-260 mg (61%) **4.2c** were obtained after chromatographic separation as orange-red crystals, mp 94°C. ^{1}H-NMR (300 MHz, $CDCl_3$) δ= 1.33, 1.38 (2*d_p, $^3J_{HH}$= 6 Hz, 12H, OC(C$\underline{H}_3$)$_2$), 4.64-4.75 ($d_p$sept, $^2J_{HP}$, 7 Hz, 2H, OC$\underline{H}$(CH$_3$)$_2$), 5.97 (br s, 1H, NH^a, NH$_2$), 7.52 (d, $^3J_{HH}$= 8.4 Hz, 2H, 3'-H, 5'-H), 7.94 (d, $^3J_{HH}$= 8.4 Hz, 2H, 2'-H, 6'-H), 9.93 (br s, 1H, NH^b, NH$_2$). ^{13}C-NMR (75.43 MHz, $CDCl_3$) δ= [23.8 (d_p, $^3J_{CP}$= 6.5 Hz), 23.9 (d_p, $^3J_{CP}$= 5 Hz, OCH(C$\underline{H}_3$)$_2$)], 72.8 (d_pd, $^2J_{CP}$= 5.5 Hz, O$\underline{C}$H(CH$_3$)$_2$), 98.5 (dp, $^1J_{CP}$= 199 Hz, C-3), 108.2 (d_p, $^3J_{CP}$= 11.5 Hz, C-5), 114.4 (s, CN), 126.7 (s, C-1'), 129.2, 129.7 (2*d, C-2', C-3', C-5', C-6'), 139.4 (s, C-4'), 157.3 (s, C-6), 162.3 (d_p, $^2J_{CP}$= 26.4 Hz, C-2), 192.5 (d_p, $^2J_{CP}$= 7.7 Hz, CS). ^{31}P-NMR (121.42 MHz, $CDCl_3$) δ= 13.3 (s). IR (KBr, tablet) ν= 3392 (w), 3215 (w), 2979 (w), 2227 (w), 1628 (s), 1589 (s), 1559 (m), 1506 (m), 1490 (w), 1457 (w), 1436 (m), 1404 (s), 1373 (s), 1282 (m), 1265 (s), 1231 (m), 1175 (m), 1091 (m), 1012 (br s), 893 (m), 874 (m), 836 (w), 823 (w), 788 (w), 743 (w), 714 (w), 668 (w), 588 (w), 506 (w), 471 (w), 444 (w), 419 (w), 411 (w), 405 (w). MS (70 eV, 133°C) m/z (%)= 427 (8), 426 (M^+, 24), 383 (M^+ - $C_3H_7^+$, 31), 139 ($ClC_6H_4CO^+$, 100), 111 ($ClC_6H_4^+$, 16), 75 ($C_6H_3^+$, 3). UV (MeCN) λ_{max} (log ε)= 254 (4.20), 301 (4.44), 322 (3.83, sh), 371 (3.57, sh). Anal. Calcd for

$C_{18}H_{20}N_2O_4ClPS$: C, 50.65; H, 4.72; N, 6.56; S, 7.51. Found: C, 50.41; H, 4.60; N, 6.53; S, 7.29.

Orange-red needles of **4.2c** with the space group C 2/c (# 15 Int. Tables) were obtained by recrystallization from chloroform / n-hexane: $C_{18}H_{20}N_2O_4ClPS*2.5\ H_2O$, mol. weight= 426.51 g mol^{-1}, ρ_{calcd}= 1.351 g cm^{-3}. The unit cell parameters were a= 22.247 (3) Å, b= 9.600 (3) Å, c= 22.272 (3) Å, β= 102.69 (2)°, V= 4640.4 (30) Å, μ= 3.526 cm^{-1} (Mo K_α), Z= 8 (no absorption correction was applied).
A total of 4547 unique reflections were recorded, of which 1966 were observed ($I \geq 3.0\ \sigma(I)$) on a Siemens P4 diffractometer using a graphite-monochromated Mo K_α radiation (λ= 0.7107 Å).

The structure was solved by direct phase determination methods and refined with isotropic hydrogen atoms as riding groups, 299 parameters (SHELXTL-PLUS by G. M. Sheldrick) on a SGI IRIS Indigo to a final R= 0.057, R_W= 0.66, maximum residual electron density 0.12 (4) e Å. Atomic coordinates are given in Table 1, bond lengths in Table 2, bond angles in Table 3 and torsion angles in Table 4.

Table 1: Atomic coordinates and isotropic thermal parameters of hydrogen atoms and non-hydrogen atoms of **4.2c**

Atom	x	y	z	$U_{iso} \cdot \frac{10^2}{Å^2}$
H8	-0.078(2)	-0.260(5)	-0.007(2)	4(1)
H9	-0.145(3)	-0.418(7)	-0.051(3)	10(2)
H12	-0.066(2)	-0.689(4)	0.069(2)	3(1)
H13	0.011(2)	-0.540(5)	0.118(2)	6(1)
H31	0.247(2)	-0.065(7)	0.115(3)	10(2)
H32	0.131(2)	-0.078(6)	0.302(2)	7(1)

H2*A*	0.159(2)	-0.444(5)	0.179(2)	5(1)
H2*B*	0.195(2)	-0.321(6)	0.207(2)	8(2)
H311	0.2486	0.0716	0.0269	14
H312	0.1833	0.0759	0.0408	14
H313	0.2290	0.1973	0.0620	14
H314	0.3407	0.0242	0.1142	17
H315	0.3235	0.1490	0.1514	17
H316	0.3291	0.0006	0.1797	17
H321	0.0687	0.0845	0.3334	23
H322	0.0977	0.2080	0.3048	23
H323	0.0566	0.1007	0.2625	23
H324	0.1747	0.0099	0.3910	23
H325	0.2252	-0.0174	0.3543	23
H326	0.2035	0.1335	0.3624	23

$T = \exp[-8\pi^2 U_{iso}(\sin\theta/\lambda)^2]$

Atom	*x*	*y*	*z*	$U_{eq} \cdot \frac{10^3}{\text{Å}^2}$
O1	0.0725(2)	-0.3389(4)	0.1220(2)	45(1)
C2	0.1210(2)	-0.2664(6)	0.1562(3)	43(2)
C3	0.1213(2)	-0.1229(6)	0.1578(3)	39(1)
C4	0.0694(2)	-0.0473(6)	0.1247(3)	39(1)
C5	0.0181(2)	-0.1338(6)	0.0905(3)	40(1)
C6	0.0209(2)	-0.2731(6)	0.0896(3)	39(2)
N2′	0.1626(2)	-0.3529(5)	0.1839(3)	60(2)
S4′	0.06102(7)	0.1243(2)	0.12275(8)	53.5(4)
C5′	-0.0368(3)	-0.0587(7)	0.0598(3)	51(2)
N5″	-0.0799(3)	-0.0008(6)	0.0368(3)	84(2)
P3′	0.18796(7)	-0.0354(2)	0.20203(8)	50.0(4)
O3′	0.2334(2)	-0.1411(5)	0.2307(2)	73(1)
O31′	0.2125(2)	0.0719(4)	0.1602(2)	54(1)
O32′	0.1686(2)	0.0706(5)	0.2473(2)	56(1)
C7	-0.0253(2)	-0.3768(6)	0.0602(2)	38(1)

C8	-0.0730(3)	-0.3436(7)	0.0111(3)	54(2)
C9	-0.1170(3)	-0.4401(7)	-0.0141(3)	54(2)
C10	-0.1136(2)	-0.5713(6)	0.0104(3)	44(2)
C11	-0.0652(3)	-0.6082(6)	0.0574(3)	53(2)
C12	-0.0216(3)	-0.5116(6)	0.0818(3)	48(2)
C31″	0.2477(3)	0.0268(8)	0.1158(3)	70(2)
C32″	0.1431(3)	0.0241(8)	0.2984(3)	79(2)
C31″A	0.2250(4)	0.097(1)	0.0581(4)	110(3)
C31″B	0.3138(3)	0.053(1)	0.1414(4)	147(4)
C32″A	0.0867(5)	0.105(2)	0.2986(5)	186(5)
C32″B	0.1889(5)	0.041(2)	0.3556(4)	208(6)
Cl10′	-0.17067(8)	-0.6916(2)	-0.01904(9)	72.2(5)
Ow1	0.1592(2)	0.3632(5)	0.1819(3)	120(2)
Ow2	0.0638(2)	0.4573(7)	0.2526(2)	115(2)
Ow3	0.500	0.2319(7)	0.250	118(2)

$U_{eq} = \frac{1}{3} \sum \sum U_{ij} \, a_i \cdot a_j \, a_i^* \, a_j^*$

Table 2: Bond distances (in Å) of **4.2c**

O1 – C2	1.367(6)	P3′ – O32′	1.560(5)
O1 – C6	1.368(6)	O31′ – C31″	1.456(9)
C2 – C3	1.379(7)	O32′ – C32″	1.447(9)
C2 – N2′	1.295(7)	Cl10′– C10	1.735(6)
C3 – C4	1.424(7)	C7 – C8	1.383(7)
C3 – P3′	1.798(5)	C7 – C12	1.377(8)
C4 – C5	1.480(7)	C8 – C9	1.376(8)
C4 – S4′	1.657(6)	C9 – C10	1.368(9)
C5 – C6	1.340(8)	C10 – C11	1.374(8)
C5 – C5′	1.454(8)	C11 – C12	1.365(8)
C6 – C7	1.477(8)	C31″ – C51″A	1.44(1)
C5′ – N5″	1.129(8)	C31″ – C31″B	1.48(1)
P3′ – O3′	1.475(4)	C32″ – C32″A	1.48(1)

P3′ – O31′	1.565(5)	C32″ – C32″*B*	1.46(1)
N2′ ··· O3′	2.641(6)	N2′ ··· Ow1	2.727(7)

In parentheses e.s.d.'s in units of the least significant digits.

Table 3: Bond angles (in °) of **4.2c**

C2 – O1 – C6	121.8(4)	O3′ – P3′ – O32′	115.4(3)
O1 – C2 – C3	121.5(5)	O31′ – P3′ – O32′	97.9(2)
O1 – C2 – N2′	109.5(5)	P3′ – O31′ – C31″	121.2(4)
C3 – C2 – N2′	129.0(5)	P3′ – O32′ – C32″	121.2(4)
C2 – C3 – C4	119.8(5)	C6 – C7 – C8	122.3(5)
C2 – C3 – P3′	118.7(4)	C6 – C7 – C12	119.7(5)
C4 – C3 – P3′	121.5(4)	C8 – C7 – C12	118.1(5)
C3 – C4 – C5	115.2(5)	C7 – C8 – C9	121.4(6)
C3 – C4 – S4′	126.5(4)	C8 – C9 – C10	119.0(5)
C5 – C4 – S4′	118.3(4)	Cl10′– C10 – C9	119.3(4)
C4 – C5 – C6	122.3(5)	Cl10′– C10 – C11	120.2(5)
C4 – C5 – C5′	116.0(5)	C9 – C10 – C11	120.5(5)
C6 – C5 – C5′	121.7(5)	C10 – C11 – C12	119.9(6)
O1 – C6 – C5	119.3(5)	C7 – C12 – C11	121.0(5)
O1 – C6 – C7	110.1(5)	O31′ – C31″ – C31″*A*	109.4(6)
C5 – C6 – C7	130.5(5)	O31′ – C31″ – C31″*B*	108.9(6)
C5 – C5′ – N5″	178.9(7)	C31″*A* – C31″ – C31″*B*	112.7(7)
C3 – P3′ – O3′	108.7(3)	O32′ – C32″ – C32″*A*	108.6(7)
C3 – P3′ – O31′	109.5(2)	O32′ – C32″ – C32″*B*	109.4(7)
C3 – P3′ – O32′	110.3(3)	C32″*A* – C32″ – C32″*B*	111.7(9)
O3′ – P3′ – O31′	114.5(3)		
N2′ – H2*A* ··· Ow1	171(3)	N2′ – H2*B* ··· O3′	139(5)

In parentheses e.s.d.'s in units of the least significant digits.

Table 4: Torsion angles (in °) of **4.2c**

C6 – O1 – C2 – C3	-2.7(7)
C2 – O1 – C6 – C5	1.3(7)
O1 – C2 – C3 – C4	2.0(8)
N2′ – C2 – C3 – P3′	1.7(8)
C2 – C3 – C4 – C5	0.0(8)
P3′ – C3 – C4 – S4′	-1.6(7)
C2 – C3 – P3′ – O3′	0.0(5)
C4 – C3 – P3′ – O31′	-54.3(5)
C4 – C3 – P3′ – O32′	52.4(5)
C3 – C4 – C5 – C6	-1.4(7)
C3 – C4 – C5 – C5′	176.1(4)
S4′ – C4 – C5 – C5′	-2.4(6)
C4 – C5 – C6 – O1	0.8(8)
C4 – C5 – C6 – C7	178.1(5)
C5′ – C5 – C6 – O1	-176.6(4)
C5′ – C5 – C6 – C7	0.7(9)
O1 – C6 – C7 – C12	19.8(7)
C5 – C6 – C7 – C8	22.1(9)
C3 – P3′ – O31′ – C31″	-76.8(4)
O3′ – P3′ – O31′ – C31″	45.5(5)
C3 – P3′ – O32′ – C32″	67.1(5)
O3′ – P3′ – O32′ – C32″	-56.6(5)
C12 – C7 – C8 – C9	2.5(8)
C8 – C7 – C12 – C11	-2.9(8)
C7 – C8 – C9 – C10	0.5(9)
C8 – C9 – C10 – C11	-3.4(9)
C9 – C10 – C11 – C12	3.0(9)
C10 – C11 – C12 – C7	0.1(9)

In parentheses e.s.d.'s in units of the least significant digits.

2-Amino-5-cyano-6-*tert*-butyl-4-thioxo-4*H*-pyran-3-ylphosphonic acid diisopropyl ester (**4.3c**)

-180 mg (48%) **4.3c** were obtained as yellow-orange crystals after

chromatographic separation, mp 73-74°C. ^{1}H-NMR (300 MHz, $CDCl_3$) δ= 1.34, 1.38 (2*d_p, $^3J_{HH}$= 6.9 Hz, 12H, OCH($C\underline{H}_3$)$_2$), 1.49 (s, 9H, ($C\underline{H}_3$)$_3$C), 4.61-4.72 ($d_p$sept, $^2J_{HP}$= 7.1 Hz, 2H, OC$\underline{H}$(CH_3)$_2$), 5.75 (br s, 1H,NH^a, NH_2), 9.78 (br s, 1H, NH^b, NH_2). ^{13}C-NMR (75.43 MHz, $CDCl_3$) δ= [23.2 (d_p, $^3J_{CP}$= 6.4 Hz), 23.5 (d_p, $^3J_{CP}$= 5.1 Hz, OCH($\underline{C}H_3$)$_2$)], 27.5 (s, ($\underline{C}H_3$)$_3$C), 36.9 (s, (CH_3)$_3\underline{C}$), 72.2 (d_pd, $^2J_{CP}$= 5.4 Hz, O$\underline{C}$H(CH_3)$_2$), 97.5 (d_p, $^1J_{CP}$= 200 Hz, C-3), 108.3 (d_p, $^3J_{CP}$= 11.9 Hz, C-5), 113.6 (s, CN), 161.5 (d_p, $^2J_{CP}$= 21.2 Hz, C-2), 170.9 (s, C-6), 193.8 (d_p, $^2J_{CP}$= 8 Hz, CS). ^{31}P-NMR (121.42 MHz, $CDCl_3$) δ= 13.5 (s). IR (KBr, tablet) ν= 3265 (w), 3137 (w), 2977 (w), 2228 (w), 1627 (s), 1587 (m), 1559 (w), 1521 (w), 1506 (w), 1496 (w), 1465 (w), 1394 (m), 1362 (m), 1270 (m), 1229 (w), 1186 (w), 1101 (w), 1013 (br s), 900 (m), 821 (w), 777 (w), 668 (w), 609 (w), 545 (w), 443 (w), 419 (w), 408 (w). MS (70 eV, 142°C) m/z (%)= 373 (7), 372 (M^+, 38), 330 (M^+ - $C_3H_6^+$, 19), 57 ($C_4H_9^+$, 100). UV (MeCN) λ_{max} (log ε)= 239 (4.46), 281 (4.24), 328 (3.71, sh). Anal. Calcd for $C_{16}H_{25}N_2O_4PS$: C, 51.60; H, 6.77; N, 7.52; S, 8.61. Found: C, 51.38; H, 6.74; N, 7.24; S, 8.57.

2-Amino-5-cyano-6-*p*-tolyl-4-thioxo-4*H*-pyran-3-ylphosphonic acid diisopropyl ester (**4.4c**)

-230 mg (56%) **4.4c** were obtained as orange-red crystals after chromatographic separation, mp 105-106°C. ^{1}H-NMR (300 MHz, $CDCl_3$) δ= 1.34, 1.38 (2*d_p, $^3J_{HH}$= 6.3 Hz, 12 Hz, OCH($C\underline{H}_3$)$_2$), 2.45 (s, 3H, $C_6H_4C\underline{H}_3$), 4.65-4.76 ($d_p$sept, $^2J_{HP}$= 7.5 Hz, OC$\underline{H}$(CH_3)$_2$), 5.62 (br s, 1H, NH^a, NH_2), 7.32-7.35 (d, $^3J_{HH}$= 8.4 Hz, 2H, 3'-H, 5'-H), 7.86-7.89 (d, $^3J_{HH}$= 8.4 Hz, 2H, 2'-H, 6'-H), 9.92 (br, s, 1H,

NH^b, NH_2). ^{13}C-NMR (90.56 MHz, $CDCl_3$) δ= 21.7 (s, $C_6H_4\underline{C}H_3$), [23.8 (d_p, $^3J_{CP}$= 5 Hz), 24.0 (d_p, $^3J_{CP}$= 4 Hz, $OCH(\underline{C}H_3)_2$)], 72.8 (d_pd, $^2J_{CP}$= 5.8 Hz, $O\underline{C}H(CH_3)_2$), 98.3 (d_p, $^1J_{CP}$= 197 Hz, C-3), 108.5 (d_p, $^3J_{CP}$= 12.1 Hz, C-5), 114.9 (s, CN), 125.6 (s, C-1'), 128.5, 129.8 (2*d, C-2', C-3', C-5', C-6'), 144.2 (s, C-4'), 158.8 (s, C-6), 162.5 (d_p, $^2J_{CP}$= 26.4 Hz, C-2), 192.6 (d_p, $^2J_{CP}$= 6.9 Hz, CS). ^{31}P-NMR (145.79 MHz, $CDCl_3$) δ= 14.1 (s). IR (KBr, tablet) ν= 3492 (w), 3380 (w), 3010 (w), 2979 (w), 2921 (w), 2225 (w), 1623 (s), 1603 (w), 1591 (m), 1559 (w), 1539 (w), 1506 (w), 1494 (w), 1457 (m), 1436 (w), 1373 (s), 1265 (s), 1237 (m), 1172 (w), 1017 (br s), 971 (w), 894 (w), 824 (w), 742 (w), 668 (w), 607 (w), 563 (w), 469 (w), 439 (w), 419 (w), 402 (w). MS (70 eV, 189°C) m/z (%)= 407 (6), 406 (M^+, 28), 364 (M^+ - $C_3H_6^+$, 9), 119 ($C_8H_7O^+$, 100), 91 ($C_7H_7^+$, 46), 65 ($C_5H_5^+$, 7). UV (MeCN) λ_{max} (log ε)= 255 (4.21), 302 (4.42), 322 (3.84), 366 (3.58). Exact mass calcd for $C_{19}H_{23}N_2O_4PS$: 406.1118. Found: 406.1116.

2-Amino-5-cyano-6-furoyl-4-thioxo-4*H*-pyran-3-ylphosphonic acid diisopropyl ester (**4.5c**)

-250 mg (65%) **4.5c** were obtained after chromatographic separation as orange-red crystals, mp 75-76°C. ^{1}H-NMR (300 MHz, $CDCl_3$) δ= 1.31, 1.37 (2*d_p, $^3J_{HH}$= 6.2 Hz, 12H, $OCH(C\underline{H}_3)_2$), 4.64-4.74 ($d_p$sept, $^2J_{HP}$= 7.3 Hz, 2H, $OC\underline{H}(CH_3)_2$), 5.91 (br s, 1H, NH^a, NH_2), 6.69 (d, $^3J_{HH}$= 3.9 Hz, 1H, 5'-H), 7.67, 7.77 (2*d, $^3J_{HH}$= 3.9 Hz, 2H, 3'-H, 4'-H), 9.95 (br s, 1H, NH^b, NH_2). ^{13}C-NMR (62.89 MHz, $CDCl_3$) δ= [23.8 (d_p, $^3J_{CP}$, 6.2 Hz), 23.9 (d_p, $^3J_{CP}$= 5.1 Hz, $OCH(\underline{C}H_3)_2$)], 72.8 (d_pd, $^2J_{CP}$= 5.9 Hz, $O\underline{C}H(CH_3)_2$), 97.9 (d_p, $^1J_{CP}$= 197 Hz,

C-3), 108.4 (d_p, $^3J_{CP}$= 11.5 Hz, C-5), 113.6 (s, C-3'), 114.2 (s, CN), 119.9 (s, C-4'), 142.4 (s, C-2'), 147.8 (s, C-5'), 148.5 (s, C-6), 162.0 (d_p, 26.8 Hz, C-2), 192.6 (d_p, $^2J_{CP}$= 7.3 Hz, CS). ^{31}P-NMR (121.42 MHz, $CDCl_3$) δ= 13.6 (s). IR (KBr, tablet) ν= 3284 (w), 3128 (w), 2979 (w), 2923 (w), 2228 (w), 1635 (s), 1600 (w), 1559 (w), 1541 (w), 1506 (w), 1465 (w), 1386 (m), 1371 (m), 1286 (m), 1247 (s), 1179 (m), 1102 (w), 1071 (w), 1002 (br s), 975 (w), 920 (w), 884 (w), 848 (w), 821 (w), 760 (w), 738 (w), 668 (w), 589 (w), 542 (w), 497 (w), 436 (w), 407 (w). MS (70 eV, 150°C) m/z (%)= 383 (10), 382 (M^+, 50), 340 (M^+ - $C_3H_6^+$, 7), 95 ($C_5H_3O_2^+$, 100), 67 ($C_4H_3O^+$, 28). UV (MeCN) λ_{max} (log ε)= 265 (4.19), 310 (4.40), 351 (3.83, sh), 402 (3.57, sh). Anal. Calcd for $C_{16}H_{19}N_2O_5PS$: C, 50.26; H, 5.01; N, 7.32; S, 8.38. Found: C, 50.33; H, 5.14; N, 7.37; S, 8.52.

2-Amino-5-cyano-6-phenyl-4-thioxo-4*H*-pyran-3-ylphenylphosphinic acid ethyl ester (**5.1d**)

-210 mg (53%) **5.1d** were obtained as orange-red crystals after chromatographic separation, mp 125-127°C. ^{1}H-NMR (250.13 MHz, $CDCl_3$) δ= 1.22 (t_p, $^3J_{HH}$= 7.1 Hz, $OCH_2\underline{C}H_3$), 4.14-4.33 (m, 2H, $OC\underline{H}_2CH_3$), 6.01 (br s, 1H, NH^a, NH_2), 7.39-7.98 [(2*m, 10H, 2'-H, 3'-H, 4'-H, 5'-H, 6'-H), $PC_6\underline{H}_5$], 9.70 (br s, 1H, NH^b, NH_2). ^{13}C-NMR (90.56 MHz, $CDCl_3$) δ= 16.5 (t_p, $^3J_{CP}$= 7.6 Hz, $OCH_2\underline{C}H_3$), 61.8 (d_pt, $^2J_{CP}$= 7.2 Hz, $O\underline{C}H_2CH_3$), 98.5 (d_p, $^1J_{CP}$= 141 Hz, C-3), 108.5 (d_p, $^3J_{CP}$= 9.1 Hz, C-5), 114.5 (s, CN), 127.8 (d, C-1'a), 128.5 (s, C-1'), 129.0, 129.5 (2*d, C-2'a, C-3'a, C-5'a, C-6'a), 132.3 (d, C-4'a), 133.1 (s, C-4'), 159.1 (s, C-6), 163.2 (d_p, $^2J_{CP}$= 20 Hz, C-2), 192.6 (d_p, $^2J_{CP}$= 9.7 Hz, CS). ^{31}P-NMR (145.79 MHz, $CDCl_3$) δ= 33.62 (s). IR (KBr, tablet) ν= 3411 (w), 3066 (w), 2977 (w), 2944 (w),

2228 (w), 1627 (s), 1601 (w), 1572 (m), 1565 (w), 1559 (w), 1540 (w), 1533 (w), 1521 (w), 1506 (w), 1496 (w), 1457 (w), 1437 (w), 1419 (w), 1375 (s), 1266 (s), 1234 (m), 1161 (m), 1116 (m), 1034 (br s), 997 (w), 877 (m), 772 (w), 739 (w), 719 (w), 691 (w), 668 (w), 646 (w), 573 (w), 543 (w), 504 (w), 443 (w), 427 (w), 419 (w), 408 (w). MS (70 eV, 235°C) m/z (%)= 397 (8), 396 (M^+, 36), 105 ($C_6H_5CO^+$, 100), 77 ($C_6H_5^+$, 98), 51 ($C_4H_3^+$, 11). UV (MeCN) λ_{max} (log ε)= 252 (4.30), 300 (4.42), 324 (4.26, sh), 370 (3.72, sh). Anal. Calcd for $C_{20}H_{17}N_2O_3PS$: C, 60.58; H, 4.32; N, 7.09; S, 8.08. Found: C, 60.31; H, 4.21; N, 6.91; S, 7.90.

2-Amino-5-cyano-6-(4'-chlorophenyl)-4-thioxo-4*H*-pyran-3-ylphenylphosphinic acid ethyl ester (**5.2d**)

-270 mg (68%) **5.2d** orange-red crystals were obtained after chromatographic separation, mp 182-183°C. ^{1}H-NMR (250.13 MHz, $CDCl_3$) δ= 1.44 (t_p, $^3J_{HH}$= 7 Hz, 3H, $OCH_2\underline{C}H_3$), 4.10-4.30 (m, 2H, $OC\underline{H}_2CH_3$), 5.92 (br s, 1H, NH^a, NH_2), 7.44-7.47 (d, $^3J_{HH}$= 8.1 Hz, 2H, 3'-H, 5'-H), 7.88-7.92 (d, $^3J_{HH}$= 8.1 Hz, 2H, 2'-H, 6'-H), 7.40-7.97 (m, 5H, $P\underline{C}_6\underline{H}_5$), 10.55 (br s, 1H, NH^b, NH_2), ^{13}C-NMR (90.56 MHz, $CDCl_3$) δ= 16.5 (t_p, $^3J_{CP}$= 7.6 Hz, $OCH_2\underline{C}H_3$), 61.8 (d_pt, $^2J_{CP}$= 7.2 Hz, $O\underline{C}H_2CH_3$), 98.6 (d_p, $^1J_{CP}$= 140 Hz, C-3), 108.6 (d_p, $^3J_{CP}$= 9.1 Hz, C-5), 114.3 (s, CN), 126.8 (s, C-1'), 127.9 (d, C-1'a), 129.0, 129.8 (2*d, C-2'a, C-3'a, C-5'a, C-6'a), 129.1, 129.5 (2*d, C-2', C-3', C-5', C-6'), 132.4 (d, C-4'a), 139.6 (s, C-4'), 157.9 (s, C-6), 163.1 (d_p, $^2J_{CP}$= 19.8 Hz, C-2), 192.3 (d_p, $^2J_{CP}$= 9.6 Hz, CS). ^{31}P-NMR (145.79 MHz, $CDCl_3$) δ= 33.70 (s). IR (KBr, tablet) ν= 3444 (w), 3060 (w), 2988 (w), 2922 (w), 2228 (w), 1628 (s), 1590 (m), 1559 (w), 1539 (w), 1521

(w), 1506 (w), 1490 (m), 1457 (w), 1437 (m), 1374 (m), 1282 (m), 1265 (m), 1230 (m), 1153 (m), 1117 (m), 1093 (m), 1035 (br s), 1013 (m), 967 (m), 878 (m), 834 (m), 820 (w), 742 (m), 716 (w), 691 (m), 668 (w), 581 (m), 546 (w), 507 (w), 450 (w), 428 (w), 422 (w), 413 (w), 404 (w). MS (70 eV, 201°C) m/z (%)= 431 (10), 430 (M^+, 22), 139 ($ClC_6H_4CO^+$, 100), 111 ($ClC_6H_4^+$, 38), 75 ($C_6H_3^+$, 34). UV (MeCN) λ_{max} (log ε)= 254 (4.30), 302 (4.45), 324 (4.27, sh), 380 (3.73, sh). Exact mass calcd for $C_{20}H_{16}N_2O_3ClPS$: 430.5894. Found: 430.5892.

General procedure for preparation of 2-*tert*-Butoxycarbonylaminophosphono-phosphino substituted γ-thiapyrones (**6**/**7**)

To a solution of 1 mmol phosphono-phosphino substituted γ-thiapyrones (**4**/**5**) in CH_2Cl_2 (15 mL) was added 12.3 mg (0.1 mmol) of DMAP and 163.5 mg (1.5 mmol) of $(Boc)_2O$. The reaction mixture was stirred under argon atmosphere for 12-14 h at rt. After evaporation of the solvent, the residue was dissolved in 50 mL of ether and 1 M $KHSO_4$ (20 mL). The etheral phase was washed with water (20 mL), 1 M $NaHCO_3$ (20 mL) and NaCl (saturated) and dried over anhydrous $MgSO_4$. After chromatographic separation (silica gel // ether) the compounds (**6**/**7**) were isolated in moderate yields (55-65%).

2-*tert*-Butoxycarbonylamino-5-cyano-6-(4'-chlorophenyl)-4-thioxo-4*H*-pyran-3-ylphosphonic acid dimethyl ester (**6.2a**)

-260 mg (55%) **6.2a** were obtained after chromatographic separation as orange-light brown crystals, mp 153-154°C. ^{1}H-NMR (300 MHz, $CDCl_3$) δ= 1.55 (s, 9H,

($C\underline{H}_3)_3C$), 3.82, 3.86 (d_p, $^3J_{HP}$= 12 Hz, 6H, $OC\underline{H}_3$), 7.59-7.64 (d, $^3J_{HH}$= 8.7 Hz, 2H, 3'-H, 5'-H), 8.32-8.36 (d, $^3J_{HH}$= 8.7 Hz, 2H, 2'-H, 6'-H), 11.98 (br s, 1H, NH). ^{13}C-NMR (90.56, $CDCl_3$) δ= 27.9 (s, $(\underline{C}H_3)_3C$), 54.1 (d_p, $^2J_{CP}$= 6.2 Hz, $O\underline{C}H_3$), 84.0 (s, $(CH_3)_3\underline{C}$), 101.1 (d_p, $^1J_{CP}$= 198 Hz, C-3), 109.3 (d_p, $^3J_{CP}$= 11.5 Hz, C-5), 114.2 (s, CN), 126.2 (s, C-1'), 129.7, 130.4 (2*d, C-2', C-3', C-5', C-6'), 140.4 (s, C-4'), 148.0 (s, COO), 158.2 (s, C-6), 159.0 (d_p, $^2J_{CP}$= 24 Hz, C-2), 194.5 (d_p, $^2J_{CP}$= 6.5 Hz, CS). ^{31}P-NMR (121.42 MHz, $CDCl_3$) δ= 17.9 (s). IR (KBr, tablet) ν= 3446 (w), 3007 (w), 2985 (w), 2958 (w), 2230 (w), 1755 (s), 1734 (w), 1718 (w), 1700 (w), 1617 (s), 1559 (m), 1540 (w), 1516 (w), 1507 (w), 1495 (w), 1472 (w), 1457 (w), 1400 (w), 1369 (m), 1353 (m), 1237 (s), 1141 (s), 1100 (w), 1035 (s), 1001 (w), 871 (w), 837 (w), 821 (w), 761 (w), 735 (w), 668 (w), 661 (w), 590 (w), 562 (w), 512 (w), 481 (w), 437 (w), 431 (w), 418 (w), 408 (w) MS (70 eV, 163°C) m/z (%)= 471 (2), 470 (M^+, 10), 369 (M^+ - $C_5H_9O_2^+$, 20), 139 ($ClC_6H_4CO^+$, 21), 111 ($ClC_6H_4^+$, 36), 75 ($C_6H_3^+$, 23), 57 ($C_4H_9^+$, 100). UV (MeCN) λ_{max} (log ε)= 262 (4.18), 305 (4.38), 328 (4.22, sh), 372 (3.88, sh).
Exact mass calcd for $C_{19}H_{20}N_2O_6ClPS$: 470.0469. Found: 470.0468.

2-*tert*-Butoxycarbonylamino-5-cyano-6-*tert*-butyl-4-thioxo-4*H*-pyran-3-ylphosphonic acid dimethyl ester (**6.3a**)

-150 mg (36%) **6.3a** were obtained as light orange crystals after chromatographic separation, mp 168-169°C. ^{1}H-NMR (300 MHz, $CDCl_3$) δ= 1.48 (s, 9H, $(C\underline{H}_3)_3C$), 1.56 (s, 9H, $(C\underline{H}_3)_3$), 3.75, 3.80 (d_p, $^3J_{HP}$= 12 Hz, 6H, $OC\underline{H}_3$), 11.90 (s, 1H, NH). ^{13}C-NMR (90.56 MHz, $CDCl_3$) δ= 27.6 (s, $(\underline{C}H_3)_3C$), 27.9 (s, $(\underline{C}H_3)_3C$), 37.5 (s, $(CH_3)_3\underline{C}$), 53.3 (d_p, $^2J_{CP}$= 6.5 Hz, $O\underline{C}H_3$), 83.7 (s, $(CH_3)_3\underline{C}$), 96.8 (d_p,

$^{1}J_{CP}$= 199 Hz, C-3), 108.7 (d_p, $^{3}J_{CP}$= 11.9 Hz, C-5), 114.0 (s, CN), 148.7 (s, COO), 160.4 (d_p, $^{2}J_{CP}$= 26.1 Hz, C-2), 165.8 (s, C-6), 193.7 (d_p, $^{2}J_{CP}$= 7.5 Hz, CS). ^{31}P-NMR (145.79 MHz, $CDCl_3$) δ= 17.8 (s). IR (KBr, tablet) ν= 3447 (w), 2965 (w), 2913 (w), 2232 (w), 1761 (s), 1734 (w), 1718 (w), 1700 (w), 1616 (s), 1550 (s), 1507 (w), 1457 (w), 1432 (m), 1395 (m), 1370 (m), 1345 (w), 1232 (s), 1141 (s), 1033 (s), 907 (w), 886 (w), 852 (w), 824 (w), 761 (w), 668 (w), 662 (w), 589 (w), 539 (w), 503 (w), 482 (w), 449 (w), 437 (w), 419 (w), 410 (w), 401 (w). MS (70 eV, 186°C) m/z (%)= 417 (3), 416 (M^+, 15), 343 (M^+ - $C_4H_9O^+$, 17), 315 (M^+ - $C_5H_9O_2^+$, 28), 57 ($C_4H_9^+$, 100). UV (MeCN) λ_{max} (log ε)= 242 (4.32), 278 (3.98), 334 (4.25). Anal. Calcd for $C_{17}H_{25}N_2O_6PS$: C, 49.02; H, 6.05; N, 6.75; S, 7.69. Found: C, 48.90; H, 5.92; N, 6.49; S, 7.48.

2-*tert*-Butoxycarbonylamino-5-cyano-6-phenyl-4-thioxo-4*H*-pyran-3-ylphosphonic acid diethyl ester (**6.1b**)

-270 (58%) **6.1b** were obtained after chromatographic separation as orange-brown crystals, mp 88-89°C. ^{1}H-NMR (300 MHz, $CDCl_3$) δ= 1.33 (d_pt, $^{3}J_{HH}$= 6.9 Hz, 6H, $OCH_2\underline{C}H_3$), 1.51 (s,9H, $(\underline{C}H_3)_3C$), 4.07-4.26 (m, 4H, $O\underline{C}H_2CH_3$), 7.52-7.62 (m, 3H, 3'-H, 4'-H, 5'-H), 8.30-8.33 (d, $^{3}J_{HH}$= 8.7 Hz, 2H, 2'-H, 6'-H), 12.10 (s, 1H, NH). ^{13}C-NMR (90.56 MHz, $CDCl_3$) δ= 16.4 (d_pq, $^{3}J_{CP}$= 7 Hz, $OCH_2\underline{C}H_3$), 27.7 (s, $(\underline{C}H_3)_3C$), 64.0 (d_pt, $^{2}J_{CP}$= 4.9 Hz, $O\underline{C}H_2CH_3$), 83.6 (s, $(CH_3)_3\underline{C}$), 102.1 (d_p, $^{1}J_{CP}$= 196 Hz, C-3), 109.5 (d_p, $^{3}J_{CP}$= 11.3 Hz, C-5), 114.4 (s, CN), 127.9 (s, C-1'), 128.9, 129.3 (2*d, C-2', C-3', C-5', C-6'), 133.7 (s, C-4'), 148.1 (s, COO), 158.7 (d_p, $^{2}J_{CP}$= 24 Hz, C-2), 159.7 (s, C-6), 194.7 (d_p, $^{2}J_{CP}$= 7.2 Hz, CS). ^{31}P-NMR (121.42 MHz, $CDCl_3$) δ= 15.0 (s). IR (KBr, tablet) ν= 3455 (w),

3011 (w), 2963 (w), 2921 (w), 2229 (w), 1757 (s), 1734 (w), 1700 (w), 1616 (s), 1575 (s), 1559 (m), 1521 (m), 1506 (m), 1496 (w), 1472 (w), 1447 (w), 1419 (w), 1395 (s), 1372 (s), 1261 (s), 1231 (m), 1195 (w), 1137 (m), 1094 (m), 1026 (br s), 960 (m), 941 (w), 894 (w), 870 (w), 801 (w), 778 (m), 757 (m), 730 (w), 691 (w), 668 (w), 618 (w), 606 (w), 591 (w), 558 (w), 526 (w), 495 (w), 437 (w), 420 (w), 411 (w). MS (70 eV, 162°C) m/z (%)= 465 (4), 464 (M^+, 20), 363 (M^+ - $C_5H_9O_2^+$, 58), 105 ($C_6H_5CO^+$, 51), 77 ($C_6H_5^+$, 29), 57 ($C_4H_9^+$, 100), 41 ($C_3H_5^+$, 18). UV (MeCN) λ_{max} (log ε)= 264 (4.35), 308 (4.42), 326 (4.59), 371 (3.90, sh). Exact mass calcd for $C_{21}H_{25}N_2O_6PS$: 464.0112. Found: 464.0112.

2-*tert*-Butoxycarbonylamino-5-cyano-6-(4'-chlorophenyl)-4-thioxo-4*H*-pyran-3-ylphosphonic acid diethyl ester (**6.2b**)

-250 mg (50%) **6.2b** were obtained as orange-brown crystals after chromatographic separation, mp 143-144°C. ^{1}H-NMR (300 MHz, $CDCl_3$) δ= 1.28 (d_pt, $^3J_{HH}$= 6.9 Hz, 6H, $OCH_2\underline{C}H_3$), 1.47 (s, 9H, $(\underline{C}H_3)_3C$), 4.04-4.18 (m, 4H, $OC\underline{H}_2CH_3$), 7.48-7.51 (d, $^3J_{HH}$= 8.7 Hz, 2H, 3'-H, 5'-H), 8.25-8.28 (d, $^3J_{HH}$= 8.7 Hz, 2H, 2'-H, 6'-H), 12.00 (s, 1H, NH). ^{13}C-NMR (75.43 MHz, $CDCl_3$) δ= 15.2 (d_pq, $^3J_{CP}$= 7.2 Hz, $OCH_2\underline{C}H_3$), 26.8 (s, $(\underline{C}H_3)_3C$), 63.0 (d_pt, $^2J_{CP}$= 6 Hz, $O\underline{C}H_2CH_3$), 82.6 (s, $(CH_3)_3\underline{C}$), 101.0 (d_p, $^1J_{CP}$= 195 Hz, C-3), 108.2 (d_p, $^3J_{CP}$= 11.5 Hz, C-5), 113.1 (s, CN), 125.1 (s, C-1'), 128.4, 129.3 (2*d, C-2', C-3', C-5', C-6'), 139.0 (s, C-4'), 146.8 (s, COO), 157.1 (d_p, $^2J_{CP}$= 25.6 Hz, C-2), 157.5 (s, C-6), 193.1 (d_p, $^2J_{CP}$= 6.8 Hz, CS). ^{31}P-NMR (121.42 MHz, $CDCl_3$) δ= 15.1 (s). IR (KBr, tablet) ν= 3404 (w), 3019 (m), 2964 (w), 2923 (w), 2230 (w), 1760 (s), 1736 (w), 1698 (w), 1614 (s), 1566 (s), 1547 (w), 1519 (w), 1492 (w), 1477 (w),

1437 (w), 1415 (w), 1396 (m), 1371 (m), 1353 (w), 1261 (m), 1231 (m), 1215 (s), 1141 (m), 1097 (w), 1026 (br s), 1014 (w), 981 (w), 929 (w), 873 (w), 824 (w), 759 (w), 668 (w), 625 (w), 598 (w), 561 (w), 535 (w), 495 (w), 450 (w), 411 (w), 401 (w). MS (70 eV, 177°C) m/z (%)= 499 (3), 498 (M^+, 13), 397 (M^+ - $C_5H_9O_2^+$, 32), 139 ($ClC_6H_4CO^+$, 22), 111 ($ClC_6H_4^+$, 8), 75 ($C_6H_3^+$, 16), 57 ($C_4H_9^+$, 100). UV (MeCN) λ_{max} (log ε)= 264 (4.35), 308 (4.41), 326 (4.38), 370 (3.89, sh). Anal. Calcd for $C_{21}H_{24}N_2O_6ClPS$: C, 50.56; H, 4.84; N, 5.63; S, 6.42. Found: C, 50.32; H, 4.67; N, 5.51; S, 6.30.

2-*tert*-Butoxycarbonylamino-5-cyano-6-(4'-chlorophenyl)-4-thioxo-4*H*-pyran-3-ylphosphonic acid diisopropyl ester (**6.2c**)

-270 mg (51%) **6.2c** were obtained after chromatographic separation as orange-brown crystals, mp 148-149°C. ^{1}H-NMR (300 MHz, $CDCl_3$) δ= 1.33, 1.37 (2*d_p, $^3J_{HH}$= 6.3 Hz, 12H, OCH(CH_3)$_2$), 4.73-4.79 ($d_p$sept, $^2J_{HP}$= 7.5 Hz, $^3J_{HH}$= 6.2 Hz, 2H, OCH(CH_3)$_2$), 7.54-7.58 (d, $^3J_{HH}$= 9.0 Hz, 2H, 3'-H, 5'-H), 8.32-8.35 (d, $^3J_{HH}$= 9.0 Hz, 2H, 2'-H, 6'-H), 12.20 (s, 1H, NH). ^{13}C-NMR (75.43 MHz, $CDCl_3$) δ = [23.8 (d_pq, $^3J_{CP}$= 5 Hz), 23.9 (d_pq, $^3J_{CP}$= 4 Hz, OCH(CH_3)$_2$)], 27.9 (s, (CH_3)$_3$C), 73.6 (d_pd, $^2J_{CP}$= 6.3 Hz, OCH(CH_3)$_2$), 83.5 (s, (CH_3)$_3$C), 103.2 (d_p, $^1J_{CP}$= 196 Hz, C-3), 109.3 (d_p, $^3J_{CP}$= 11.5 Hz, C-5), 114.3 (s, CN), 126.2 (s, C-1'), 129.4, 130.4 (2*d, C-2', C-3', C-5', C-6'), 139.9 (s, C-4'), 148.0 (s, COO), 157.7 (s, C-6), 158.0 (d_p, $^2J_{CP}$= 24 Hz, C-2), 194.0 (d_p, $^2J_{CP}$= 6.8 Hz, CS). ^{31}P-NMR (121.42 MHz, $CDCl_3$) δ= 12.1 (s). IR (KBr, tablet) ν= 3446 (w), 3003 (w), 2918 (w), 2865 (w), 2229 (w), 1755 (s), 1733 (w), 1717 (w), 1635 (w), 1616 (s), 1564 (m), 1544 (w), 1506 (w), 1495 (w), 1456 (w), 1436 (w), 1393 (m), 1387

(m), 1351 (w), 1219 (s), 1136 (s), 1032 (br s), 993 (m), 870 (w), 839 (w), 756 (w), 668 (w), 600 (w), 591 (w), 518 (w), 437 (w), 421 (w), 416 (w), 410 (w), 406 (w), 402 (w). MS (70 eV, 174°C) m/z (%)= 527 (2), 526 (M^+, 11), 425 (M^+ - $C_5H_9O_2^+$, 10), 139 ($ClC_6H_4CO^+$, 28), 111 ($ClC_6H_4^+$, 4), 75 ($C_6H_3^+$, 13), 57 ($C_4H_9^+$, 100), 41 ($C_3H_5^+$, 22). UV (MeCN) λ_{max} (log ε)= 264 (4.25), 308 (4.40), 326 (4.30), 372 (3.89, sh). Exact mass calcd for $C_{23}H_{28}N_2O_6ClPS$: 527.0118. Found: 527.0116.

2-*tert*-Butoxycarbonylamino-5-cyano-6-*p*-tolyl-4-thioxo-4*H*-pyran-3-ylphosphonic acid diisopropyl ester (**6.4c**)

-260 mg (52%) **6.4c** were obtained as orange-brown crystals after chromatographic separation, mp 161°C. ^{1}H-NMR (300 MHz, $CDCl_3$) δ= 1.34, 1.38 (2*d_p, $^3J_{HH}$= 6.3 Hz, 12H, OCH($C\underline{H}_3$)$_2$), 1.53 (s, ($C\underline{H}_3$)$_3$C), 2.45 (s, $C_6H_4C\underline{H}_3$), 4.73-4.79 ($d_p$sept, $^2J_{HP}$= 7.6 Hz, $^3J_{HH}$= 6.3 Hz, 2H, OC$\underline{H}$(CH_3)$_2$), 7.37-7.40 (d, $^3J_{HH}$= 8.7 Hz, 2H, 3'-H, 5'-H), 8.25-8.28 (d, $^3J_{HH}$= 8.7 Hz, 2H, 2'-H, 6'-H), 12.20 (s, 1H, NH). ^{13}C-NMR (90.56 MHz, $CDCl_3$) δ= 21.8 (s, $C_6H_4\underline{C}H_3$), [23.8 (d_pq, $^3J_{CP}$= 5 Hz), 23.9 (d_pq, $^3J_{CP}$= 4 Hz, OCH($\underline{C}H_3$)$_2$)], 27.4 (s, ($\underline{C}H_3$)$_3$C), 72.7 (d_pd, $^2J_{CP}$= 5.9 Hz, O$\underline{C}$H(CH_3)$_2$), 83.5 (s, (CH_3)$_3\underline{C}$), 103.0 (d_p, $^1J_{CP}$= 196 Hz, C-3), 109.0 (d_p, $^3J_{CP}$= 11.5 Hz, C-5), 114.8 (s, CN), 125.1 (s, C-1'), 128.9, 129.6 (2*d, C-2', C-3', C-5', C-6'), 144.8 (s, C-4'), 148.3 (s, COO), 158.2 (s, C-6), 159.4 (d_p, $^2J_{CP}$= 24.3 Hz, C-2), 194.7 (d_p, $^2J_{CP}$= 7 Hz, CS). ^{31}P-NMR (121.42 MHz, $CDCl_3$) δ= 12.0 (s). 3448 (w), 3008 (w), 2980 (w), 2951 (w), 2231 (w), 1756 (s), 1734 (w), 1717 (w), 1700 (w), 1695 (w), 1653 (w), 1616 (s), 1569 (m), 1539 (w), 1506 (w), 1495 (w), 1453 (w), 1404 (w), 1373 (m), 1354 (m), 1230 (s), 1139 (s), 1101 (w), 1003 (br s), 872 (w), 823 (w), 819 (w), 760 (w), 702 (w), 668 (w), 635 (w), 602 (w),

545 (w), 503 (w), 472 (w), 443 (w), 406 (w), 402 (w). MS (70 eV, 192°C) m/z (%)= 507 (5), 506 (M^+, 19), 405 (M^+ - $C_5H_9O_2^+$, 16), 119 ($C_8H_7O^+$, 59), 91 ($C_7H_7^+$, 18), 65 ($C_5H_5^+$, 12), 57 ($C_4H_9^+$, 100). UV (MeCN) λ_{max} (log ε)= 266 (4.30), 306 (4.42), 328 (4.32), 372 (3.90, sh). Exact mass calcd for $C_{24}H_{21}N_2O_6PS$: 506.2586. Found: 506.2585.

2-*tert*-Butoxycarbonylamino-5-cyano-6-phenyl-4-thioxo-4*H*-pyran-3-ylphenyl-phosphinic acid ethyl ester (**7.1d**)

-240 mg (48%) **7.1d** were obtained as orange-brown crystals after chromatographic separation, mp 86-87°C. ^{1}H-NMR (250.13 MHz, $CDCl_3$) δ= 1.44 (t_p, $^3J_{HH}$= 7 Hz, 3H, $OCH_2C\underline{H}_3$), 1.50 (s, 9H, $(C\underline{H}_3)_3C$), 4.06-4.26 (m, 2H, $OC\underline{H}_2CH_3$), 7.36-7.96 (2*m, 10H, 2'-H, 3'-H, 4'-H, 5'-H, 6'-H), $PC_6\underline{H}_5$), 12.08 (s, 1H, NH). ^{13}C-NMR (90.56 MHz, $CDCl_3$) δ= 16.4 (t_p, $^3J_{CP}$= 7.8 Hz, $OCH_2\underline{C}H_3$), 27.8 (s, $(\underline{C}H_3)_3C$), 62.4 (d_pt, $^2J_{CP}$= 6.7 Hz, $O\underline{C}H_2CH_3$), 83.7 (s, $(CH_3)_3\underline{C}$), 102.6 (d_p, $^1J_{CP}$= 138 Hz, C-3), 108.7 (d_p, $^3J_{CP}$= 9.2 Hz, C-5), 114.3 (s, CN), 126.0 (s, C-1'), 128.0, 128.6 (2*d, C-2', C-3', C-5', C-6',), 129.8 (d, C-1'a), 130.7, 131.2 (2*d, C-2'a, C-3'a, C-5'a, C-6'a), 133.1 (d, C-4'a), 133.2 (s, C-4'), 148.9 (s, COO), 158.1 (s, C-6), 159.2 (d_p, $^2J_{CP}$= 17.7 Hz, C-2), 193.7 (d_p, $^2J_{CP}$= 9 Hz, CS). ^{31}P-NMR (145.79 MHz, $CDCl_3$) δ= 33.1 (s). IR (KBr, tablet) ν= 3447 (w), 3056 (w), 2964 (w), 2922 (w), 2233 (w), 1756 (s), 1734 (w), 1717 (w), 1700 (w), 1695 (w), 1675 (w), 1653 (w), 1616 (s), 1576 (m), 1540 (w), 1506 (w), 1496 (w), 1472 (w), 1457 (w), 1437 (m), 1394 (m), 1375 (m), 1354 (w), 1261 (s), 1228 (m), 1137 (s), 1100 (m), 1023 (br s), 871 (w), 822 (m), 800 (s), 718 (w), 685 (w), 668 (w), 583 (w), 555 (w), 502 (w), 441 (w), 425 (w), 420 (w), 414 (w), 409 (w), 403

(w). MS (70 eV, 184°C) m/z (%)= 497 (2), 496 (M^+, 5), 395 (M^+ - $C_5H_9O_2^+$, 9), 105 ($C_6H_5CO^+$, 10), 77 ($C_6H_5^+$, 6), 57 ($C_4H_9^+$, 100), 41 ($C_3H_5^+$, 23). UV (MeCN) λ_{max} (log ε)= 266 (4.32), 308 (4.48), 336 (4.30, sh), 374 (3.92, sh). Exact mass calcd for $C_{25}H_{25}N_2O_5PS$: 496.0456. Found: 496.0454.

2-*tert*-Butoxycarbonylamino-5-cyano-6-(4'-chlorophenyl)-4-thioxo-4*H*-pyran-3-ylphenylphosphinic acid ethyl ester (**7.2d**)

-220 mg (41%) **7.2d** were obtained as orange-brown crystals after chromatographic separation, mp 110-112°C. ^{1}H-NMR (250.13 MHz, $CDCl_3$) δ= 1.43 (t_p, $^3J_{HH}$= 7 Hz, 3H, $OCH_2C\underline{H}_3$), 1.51 (s, $(C\underline{H}_3)_3C$), 4.08-4.27 (m 2H, $OC\underline{H}_2CH_3$), 7.42-7.45 (d, $^3J_{HH}$= 8.7 Hz, 2H, 3'-H, 5'-H), 7.86-7.90 (d, $^3J_{HH}$= 8.7 Hz, 2'-H, 6'-H), 7.38-7.94 (m, 5H, $PC_6\underline{H}_5$), 12.12 (s, 1H, NH). ^{13}C-NMR (90.56 MHz, $CDCl_3$) δ= 16.4 (t_p, $^3J_{CP}$= 7.8 Hz, $OCH_2\underline{C}H_3$), 27.9 (s, $(\underline{C}H_3)_3C$), 62.2 (d_pt, $^2J_{CP}$= 6.7 Hz, $O\underline{C}H_2CH_3$), 83.8 (s, $(CH_3)_3\underline{C}$), 102.8 (d_p, $^1J_{CP}$= 137 Hz, C-3), 108.9 (d_p, $^3J_{CP}$= 9.2 Hz, C-5), 114.1 (s, CN), 126.3 (s, C-1'), 128.1, 128.5 (2*d, C-2', C-3', C-5', C-6'), 129.6 (d, C-1'a), 130.5, 131.9 (2*d, C-2'a, C-3'a, C-5'a, C-6'a), 132.7 (d, C-4'a), 140.2 (s, C-4'), 148.3 (s, COO), 158.4 (s, C-6), 159.1 (d_p, $^2J_{CP}$= 17.8 Hz, C-2), 193.9 (d_p, $^2J_{CP}$= 9.1 Hz, CS). ^{31}P-NMR (145.79 MHz, $CDCl_3$) δ= 33.2 (s). IR (KBr, tablet) ν= 3445 (w), 2977 (w), 2922 (w), 2866 (w), 2233 (w), 1750 (s), 1734 (w), 1717m (w), 1700 (w), 1616 (s), 1564 (m), 1541 (m), 1527 (w), 1520 (w), 1506 (w), 1495 (w), 1472 (w), 1464 (w), 1456 (w), 1436 (m), 1419 (w), 1394 (m), 1375 (m), 1350 (w), 1227 (s), 1137 (s), 1095 (w), 1036 (br s), 970 (w), 872 (w), 834 (w), 794 (w), 771 (w), 687 (w), 668 (w), 651 (w), 637 (w), 618 (w), 607 (w), 586 (w), 535 (w), 493 (w), 483 (w), 458 (w), 439 (w), 424 (w), 417 (w), 411 (w), 408 (w),

401 (w). MS (70 eV, 186°C) m/z (%)= 531 (2), 530 (M^+, 9), 430 (14), 429 (M^+ - $C_5H_9O_2^+$, 23), 139 ($ClC_6H_4CO^+$, 20), 111 ($ClC_6H_4^+$, 4), 75 ($C_6H_3^+$, 12), 57 ($C_4H_9^+$, 100), 41 ($C_3H_5^+$, 78). UV (MeCN) λ_{max} (log ε)= 268 (4.36), 312 (4.50), 340 (4.35, sh), 374 (3.89, sh). Exact mass calcd for $C_{25}H_{24}N_2O_5ClPS$: 530.0834. Found: 530.0836.

General procedure for preparation of phosphono-phosphino substituted γ-pyrones (**8**/**9**)

To a solution of 1 mmol phosphono-phosphino substituted γ-thiapyrones (**4**/**5**) in 10 mL of glacial acidic acid and 5 mL of chloroform was added 1 g of $Hg(OAc)_2$ in 5 mL of glacial acidic acid. The reaction mixture was stirred for 1 h at rt, the precipitate was filtered of and washed with 20 mL chloroform. The combined layers were concentrated and stirred with benzene (60 mL) and water (20 mL). The benzene phase was dried over anhydrous $MgSO_4$. After evaporation of the solvent, the residue was stirred with ether / n-hexane (1:1) to give colorless, light-yellow crystals of (**8**/**9**) in moderate yields (50-60%).

2-Amino-5-cyano-6-*p*-tolyl-4-oxo-4*H*-pyran-3-ylphosphonic acid dimethyl ester (**8.4a**)

-180 mg (54%) **8.4a** were obtained after recrystallisation as colorless, light-yellow crystals, mp 177-179°C. ^{1}H-NMR (250.13 MHz, $CDCl_3$) δ= 2.43 (s, 3H, $C_6H_4C\underline{H}_3$), 3.80, 3.85 (d_p, $^3J_{CP}$= 11.7 Hz, $OC\underline{H}_3$), 6.24 (br s, 1H, NH^a, NH_2), 7.32-7.35 (d, $^3J_{HH}$= 8.7 Hz, 2H, C-3', C-5'), 7.88-7.91 (d, $^3J_{HH}$= 8.7 Hz, 2H, C-2', C-

6'), 8.91 (br s, 1H, NH^b, NH_2). ^{13}C-NMR (90.56 MHz, $CDCl_3$) δ= 21.3 (s, $C_6H_4\underline{C}H_3$), 53.6 (d_p, $^2J_{CP}$= 6.4 Hz, $O\underline{C}H_3$), 83.2 (d_p, $^1J_{CP}$= 193 Hz, C-3), 98.8 (d_p, $^3J_{CP}$= 11.8 Hz, C-5), 113.9 (s, CN), 125.7 (s, C-1'), 128.7, 129.6 (2*d, C-2', C-3', C-5', C-6'), 144.4 (s, C-4'), 166.5 (s, C-6), 167.4 (d_p, $^2J_{CP}$= 22.4 Hz, C-2), 173.3 (d_p, $^2J_{CP}$= 7.6 Hz, CO). ^{31}P-NMR (145.79 MHz, $CDCl_3$) δ= 20.49 (s). IR (KBr, tablet) ν= 3377 (w), 3166 (w), 2955 (w), 2855 (w), 2228 (w), 1646 (s), 1617 (s), 1582 (m), 1539 (m), 1507 (w), 1486 (w), 1453 (w), 1419 (m), 1374 (w), 1261 (m), 1223 (w), 1025 (br s), 989 (w), 822 (m), 801 (w), 776 (w), 712 (w), 668 (w), 631 (w), 614 (w), 597 (w), 551 (w), 542 (w), 517 (w), 483 (w), 439 (w), 426 (w), 413 (w), 403 (w). MS (70 eV, 185°C) m/z (%)= 335 (7), 334 (M^+, 42), 119 ($C_8H_7CO^+$, 100), 109 ($C_2H_6O_3P^+$, 22), 91 ($C_7H_7^+$, 33), 65 ($C_5H_5^+$, 13). UV (MeCN) λ_{max} (log ε)= 226 (4.40), 248 (4.25), 298 (4.19), 326 (3.95, sh). Exact mass calcd for $C_{15}H_{15}N_2O_5P$: 334.0720. Found: 334.0721.

2-Amino-5-cyano-6-(4'-chlorophenyl)-4-oxo-4*H*-pyran-3-ylphosphonic acid diethyl ester (**8.2b**)

-190 mg (50%) **8.2b** were obtained as colorless, light-yellow crystals after recrystallisation, mp 163-164°C. ^{1}H-NMR (250.13 MHz, $CDCl_3$) δ= 1.28 (t_p, $^3J_{HH}$= 6.8 Hz, 6H, $OCH_2C\underline{H}_3$), 4.11-4.19 (m, 4H, $OC\underline{H}_2CH_3$), 6.12 (br s, 1H, NH^a, NH_2), 7.44-7.48 (d, $^3J_{HH}$= 8.4 Hz, 2H, 3'-H, 5'-H), 7.87-7.90 (d, $^3J_{HH}$= 8.4 Hz, 2H, 2'-H, 6'-H), 8.99 (br s, 1H, NH^b, NH_2). ^{13}C-NMR (62.89 MHz, $CDCl_3$) δ= 15.2 (d_pq, $^3J_{CP}$= 6.5 Hz, $OCH_2\underline{C}H_3$), 62.4 (d_pt, $^2J_{CP}$= 5.7 Hz, $O\underline{C}H_2CH_3$), 84.6 (d_p, $^1J_{CP}$= 196 Hz, C-3), 98.2 (d_p, $^3J_{CP}$= 12.5 Hz, C-5), 112.3 (s, CN), 125.9 (s, C-

1'), 127.8, 128.5 (2*d, C-2', C-3', C-5', C-6'), 138.9 (s, C-4'), 164.1 (s, C-6), 166.0 (d_p, $^2J_{CP}$= 22.7 Hz, C-2), 171.6 (d_p, $^2J_{CP}$= 7.6 Hz, CO). ^{31}P-NMR (145.79 MHz, $CDCl_3$) δ= 16.05 (s). IR (KBr, tablet) ν= 3288 (w), 3144 (w), 2963 (w), 2927 (w), 2230 (w), 1654 (s), 1617 (s), 1583 (s), 1575 (w), 1540 (m), 1506 (w), 1495 (w), 1436 (w), 1406 (w), 1375 (m), 1346 (w), 1261 (s), 1222 (m), 1171 (w), 1099 (m), 1023 (br s), 990 (w), 823 (w), 801 (w), 799 (s), 739 (w), 702 (w), 668 (w), 646 (w), 593 (w), 557 (w), 505 (w), 480 (w), 445 (w), 425 (w), 410 (w), 403 (w). MS (70 eV, 217°C) m/z (%)= 383 (5), 382 (M^+, 22), 139 ($ClC_6H_4CO^+$, 100), 111 ($ClC_6H_4^+$, 34), 75 ($C_6H_3^+$, 13). UV (MeCN) λ_{max} (log ε)= 224 (4.20), 248 (4.36), 294 (3.94), 326 (3.58, sh). Anal. Calcd for $C_{16}H_{16}N_2ClO_5P$: C, 50.20; H, 4.21; N, 7.34. Found: C, 49.98; H, 4.11; N, 7.18.

2-Amino-5-cyano-6-phenyl-4-oxo-4*H*-pyran-3-ylphosphonic acid diisopropyl ester (**8.1c**)

-230 mg (62%) **8.1c** were obtained as colorless, light yellow crystals after recrystallisation, mp 125-126°C. ^{1}H-NMR (250.13 MHz, $CDCl_3$)δ= 1.23, 1.28 (2* d, $^3J_{HH}$= 6.2 Hz, 12H, $OCH(C\underline{H}_3)_2$), 4.61-4.72 ($d_p$sept, $^2J_{HP}$= 7.4 Hz, $^3J_{HH}$= 6.2 Hz, 2H, $OCH(C\underline{H}_3)_2$), 6.20 (br s, 1H, NH^a, NH_2), 7.43-7.53 (m, 3H, 3'-H, 4'-H, 5'-H), 7.90-7.93 (d, $^3J_{HH}$= 7.2 Hz, 2H, 2'-H, 6'-H), 9.01 (br s, 1H, NH^b, NH_2). ^{13}C-NMR (90.56 MHz, $CDCl_3$)δ= [22.5 (d_pq, $^3J_{CP}$= 5Hz), 22.8 (d_pq, $^3J_{CP}$= 4Hz, $OCH(\underline{C}H_3)_2$)], 71.5 (d_pd, $^2J_{CP}$= 6Hz, $O\underline{C}H(CH_3)_2$), 84.5 (d_p, $^1J_{CP}$= 191 Hz, C-3), 98.6 (d_p, $^3J_{CP}$= 12Hz, C-5), 112.5 (s, CN), 126.8 (s, C-1'), 127.6, 128.2 (2*d, C-2', C-3', C-5', C-6'), 132.3 (d, C-4'), 165.2 (s, C-6), 165.9 (d_p, $^2J_{CP}$= 19.3Hz, C-2), 171.1 (d_p, $^2J_{CP}$= 7.5Hz, CO). ^{31}P-NMR (145.79 MHz, $CDCl_3$)δ= 13.06 (s).

IR(KBr, tablet)ν= 3291 (w), 3145 (w), 2979 (w), 2933 (w), 2231 (w), 1647 (s), 1611 (s), 1583 (s), 1559 (w), 1539 (w), 1533 (m), 1506 (w), 1496 (w), 1448 (w), 1429 (m), 1374 (m), 1261 (m), 1207 (m), 1176 (w), 1104 (m), 1001 (br s), 885 (w), 824 (w), 788 (m), 769 (m), 683 (w), 668 (w), 617 (w), 609 (w), 553 (w), 486 (w), 448 (w), 427 (w), 407 (w), 401 (w). MS (70eV, 183°C) m/z (%)= 376 (M^+, 16), 105 ($C_6H_5CO^+$, 100), 77($C_6H_5^+$, 23), 51 ($C_4H_3^+$, 3), 43 ($C_3H_7^+$, 15). UV (MeCN) λ max (log ε)= 224 (4.22), 246 (4.34), 290 (3.98), 324 (3.68, sh). Anal. Calcd for $C_{18}H_{21}N_2O_5P$: C, 57.49; H, 5.62; N, 7.46. Found: C, 57.36; H, 5.38; N, 7.29.

2-Amino-5-cyano-6-(4'-chlorophenyl)-4-oxo-4*H*-pyran-3-ylphenylphosphinic acid ethylester (**9.2b**)

-160 mg (38%) **9.2b** were obtained as colorless light yellow crystals after recrystallisation, mp 167-169°C. ^{1}H-NMR (250.13 MHz, $CDCl_3$)δ= 1.31 (t_p, $^3J_{HH}$= 7Hz, 3H, $OCH_2C\underline{H}_3$), 4.08-4.27 (m, 2H, $OC\underline{H}_2CH_3$), 5.96 (br s, 1H, NH^a, NH_2), 7.41-7.45 (d, $^3J_{HH}$= 8.7 Hz, 2H, 3'-H, 5'-H), 7.87-7.91 (d, $^3J_{HH}$= 8.7 Hz, 2H, 2'-H, 6'-H), 7.37-7.96 (m, 5H, P-$C_6\underline{H}_5$), 9.96 (br s, 1H, NH^b, NH_2). ^{13}C-NMR (62.89 MHz, $CDCl_3$)δ= 16.4 (t_p, $^3J_{CP}$= 7.5Hz, $OCH_2\underline{C}H_3$), 61.7 (d_pt, $^2J_{CP}$= 7.2Hz, $O\underline{C}H_2CH_3$), 83.6 (d_p, $^1J_{CP}$= 142Hz, C-3), 99.4 (d_p, $^3J_{CP}$= 12.2Hz, C-5), 126.6 (s, C-1'), 127.8 (d, C-1'a), 128.8, 130.1 (2*d, C-2'a, C-3'a, C-5'a, C-6'a), 129.0, 129.6 (d, C-2', C-3', C-5', C-6'), 132.6 (d, C-4'a), 140.3 (s, C-4'), 164.1 (s, C-6), 166.7 (d_p, $^2J_{CP}$= 22.8Hz, C-2), 172.4 (d_p, $^3J_{CP}$= 7.8Hz, CO. ^{31}P-NMR (145.79 MHz, $CDCl_3$)δ= 33.20 (s). IR (KBr, tablet)ν= 3285 (w), 3140 (w), 3016 (w), 2990 (w), 2937 (m), 2229 (w), 1652 (s), 1626 (s), 1559 (m), 1557 (m), 1533 (w), 1508 (w), 1494 (w), 1437 (w), 1401 (w), 1373 (m), 1285 (m), 1264 (s), 1226

(m), 1170 (w), 1098 (w), 1020 (br s), 991 (m), 821 (m), 800 (w), 798 (w), 839 (w), 701 (w), 668 (w), 645 (w), 593 (w), 556 (w), 506 (w), 481 (w), 444 (w), 424 (w), 409 (w), 403 (w). MS(70eV, 189°C) m/z (%)= 415 (3), 414 (M^+, 11), 139 ($ClC_6H_4CO^+$, 15), 111 ($ClC_6H_4^+$, 17), 77 ($C_6H_5^+$, 100), 51 ($C_4H_3^+$, 22). UV (MeCN) λ_{max} (log ε)= 224 (4.18), 248 (4.38), 294 (3.91, sh), 324 (3.61, sh). Exact mass calcd for $C_{20}H_{16}N_2ClO_4P$: 414.5640. Found: 414.5639.

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REFERENCES

1. K. Issleib, *Nachr. Chem. Tech. Lab.*, 1987, **35**, 1037 and references therein.
2. A. Kleemann and J. Engel, "Pharmazeutische WIRkstoffe: Synthesen, Patente, Anwendungen", Thieme Verlag, Stuttgart, 1982.
3. E. Schaumann and F.-F. Grabley, *Liebigs Ann. Chem.*, 1979, 1715.
4. R. Engel, *Chem. Rev.*, 1977, **77**, 349; M. Grayson and J. Griffith, "Topics in Phosphorus Chemistry", Vol. 11, Wiley Interscience, New York, 1976, pp. 297-338.

5. a) R. Neidlein, M. Jochheim, C. Krieger, and W. Kramer, *Heterocycles*, 1994, **39**, 185; b) H.G. Krug, R. Neidlein, C. Krieger, and W. Kramer, *Heterocycles*, 1994, **38**, 2695; c) H.G. Krug, R. Neidlein, R. Boese, and W. Kramer, *Heterocycles*, 1995, **41**, 721; d) M. Jochheim, H.G. Krug, R. Neidlein, and C. Krieger, *Heterocycles*, 1995, **41**, 1235.
6. K. Peseke and J. Q. Suarez, *Z. Chem.*, 1981, **21**, 406.
7. T. Eicher and S. Hauptmann, "Chemie der Heterocyclen", Thieme Verlag, Stuttgart, 1994.
8. F. H. Allen, O. Kennard, D. G. Watson, L. Brammer, A. G. Orpen, and R. Taylor, *J. Chem. Soc., Perkin Trans. II*, 1987, S1.
9. G. H. Stout and L. H. Jensen, "X-Ray Structure Determination", 2nd Edn., Wiley & Sons, New York, 1989.
10. L. Grehn and U. Ragnarsson, *Angew. Chem.*, 1985, **97**, 519.
11. L. Grehn and U. Ragnarsson, *Angew. Chem.*, 1984, **96**, 291.
12. H.-Otto Kalinowski, St. Berger and S. Braun, "^{13}C-NMR-Spektroskopie", Thieme Verlag, Stuttgart, 1984.
13. M. Hesse, H. Meier and B. Zeeh, "Spektroskopische Methoden in der Organischen Chemie", Thieme Verlag, Stuttgart, 1991.
14. a) H. Hagemann, "Methoden der Organischen Chemie (Houben-Weyl)", 4. Aufl 1952-1985, Vol. E4, S. 139; b) N. G. Kardouche and L. N. Owen, *J. Chem. Soc., Perkin Trans. I*, 1975, 754.
15. J. Staunton, "Comprehensive Organic Chemistry", Pergamon Press, Oxfort, New York, Toronto, Sydney, Paris, Frankfurt, 1979, V4 Heterocyclic Compounds, 18.3 γ-Pyrones and Chromones.

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