SYNTHESES OF PHOSPHONATO-SUBSTITUTED AZOLO[1,2,4]-TRIAZINES WITH POTENTIAL BIOMEDICAL APPLICATIONS

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Abstract- The syntheses of [1,2,4]*triazino*[4,3-*b*][1,2,4]*indazol*-3-yl-phosphonic acid dialkyl esters **(5-7)**, pyrazolo[3,2-*c*][1,2,4]triazin-3-yl-phosphonic acid dialkyl esters **(9-11)** and [1,2,4]triazolo[3,2-*c*][1,2,4]triazin-3-ylphosphonic acid dialkyl esters **(13-15)** are desribed. The treatment of 7-methylpyrazolo[1,2,4]triazin derivatives **(9c,d, 11c-e)** with *N*-bromo- or *N*-iodosuccinimide yields the corresponding 8-halogen compounds **(19a-h)**. The 8-iodo derivatives could be coupled with phenylacetylene.

INTRODUCTION

Previously[1] *at the Institute various investigations towards phosphonato-substituted heterocyclic and alicyclic compounds were carried out. We now wish to report our results concerning phosphonato-substituted azolo[1,2,4]triazines.*

[1,2,4]Triazino[4,3-*b*]indazoles[2], pyrazolo[3,2-c][1,2,4]triazines[3,4] and [1,2,4]triazolo[3,2-c][1,2,4]-triazines[3,5] are known. As analogues of the purine bases they may have a wide range of biological activity.[6] Organic phosphorus compounds like phosphono derivatives are active, for example against osteoporosis or as antibiotics like fosfomycine and others. Thus we prepared azolo[1,2,4]triazines with phosphonato substituents in position 3 by [4+2] cycloaddition using heterocyclic diazobetaines and phosphonoacetic acid derivatives and aroylmethylphosphonic acid dialkyl esters respectively.

RESULTS AND DISCUSSION

Procedures formerly described by Novinson[3] or Ege[4] failed in our case because of the lower C-H-acidity of the used phosphonates compared to malonic acid derivatives. Thus we prepared the monocarbanions of the phosphonates with NaH in anhydrous THF (1 h).This solution was

added to the solution of the diazobetaine in CH_2Cl_2.[8] The reaction mixture turned dark-red immediately and was refluxed for 4 – 12 h. Thereby the [1,2,4]triazino[4,3-*b*]indazoles **(5-7)**, pyrazolo[3,2-*c*][1,2,4]triazines **(9-11)** and [1,2,4]triazolo[3,2-*c*][1,2,4]triazines **(13-15)** with phosphonato-substitution in position 3 were obtained as crude products, which were isolated as pure solids after chromatography and recrystallisation (Scheme 1-3).

Scheme 1

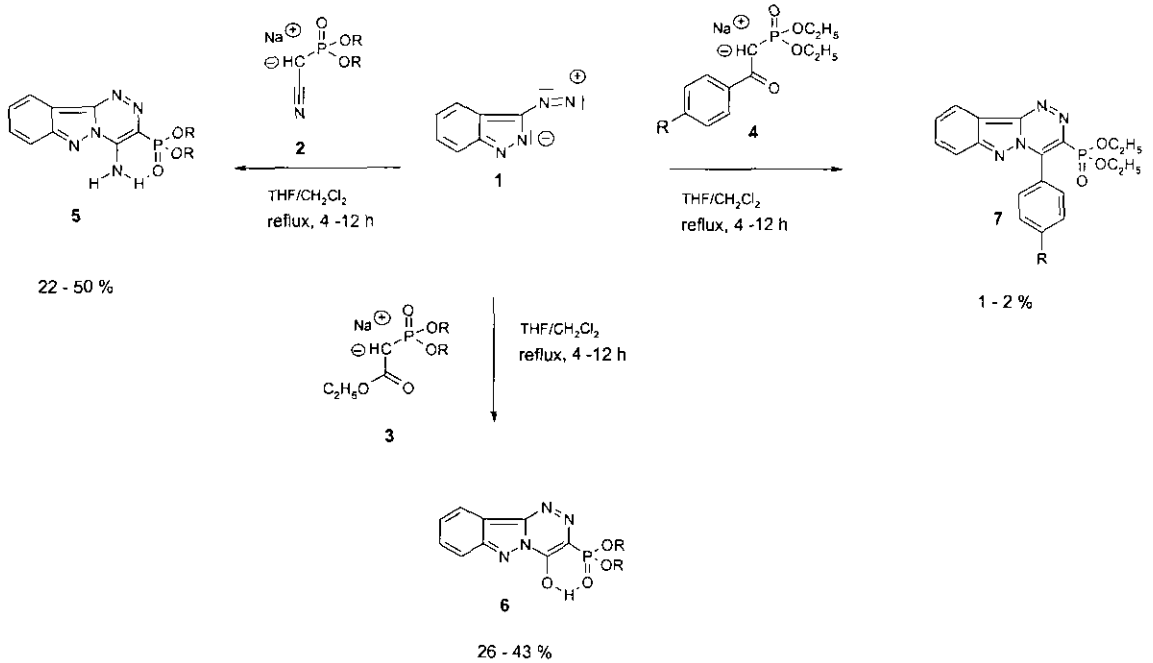


Table 1

5	R
a	CH_3
b	C_2H_5
c	*i*-C_3H_7

Table 2

6	R

a	C_2H_5
b	*i*-C_3H_7

Table 3

7	R
a	H
b	Cl

Scheme 2

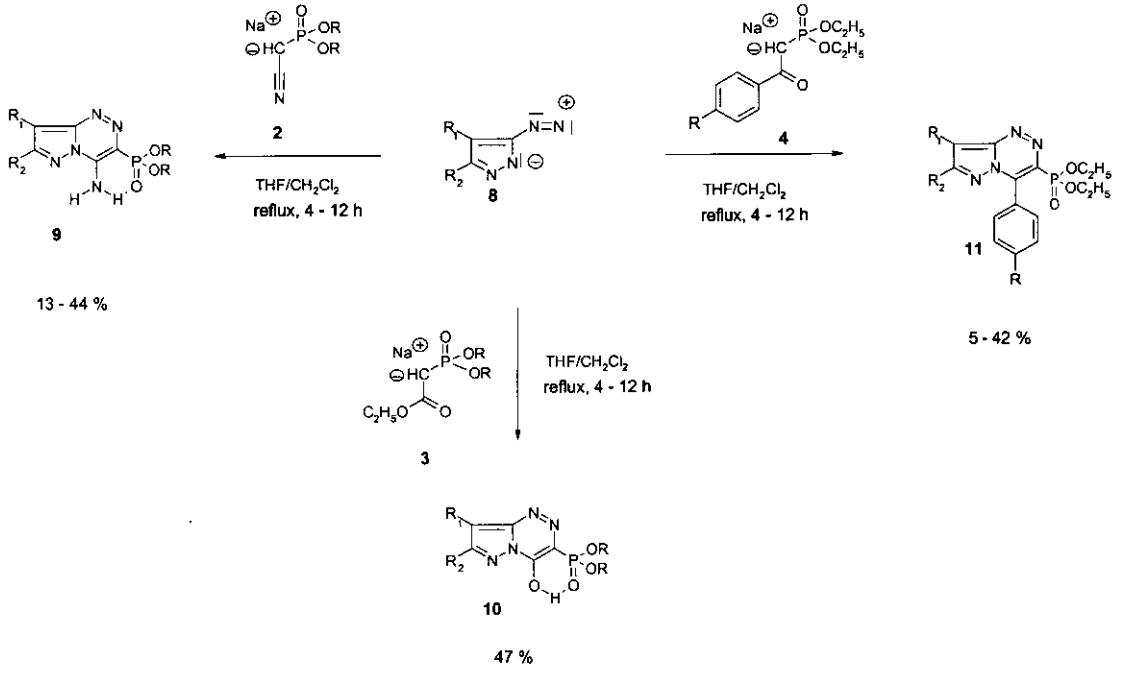


Table 4

9	R_1	R_2	R_3
a	$COOC_2H_5$	H	C_2H_5
b	$COOC_2H_5$	H	*i*-C_3H_7
c	H	CH_3	C_2H_5
d	H	CH_3	*i*-C_3H_7

Table 5

10	R_1	R_2	R
	$COOC_2H_5$	H	C_2H_5

Table 6

11	R_1	R_2	R_3
a	$COOC_2H_5$	H	H
b	$COOC_2H_5$	H	CH_3
c	H	CH_3	H
d	H	CH_3	Cl

Scheme 3

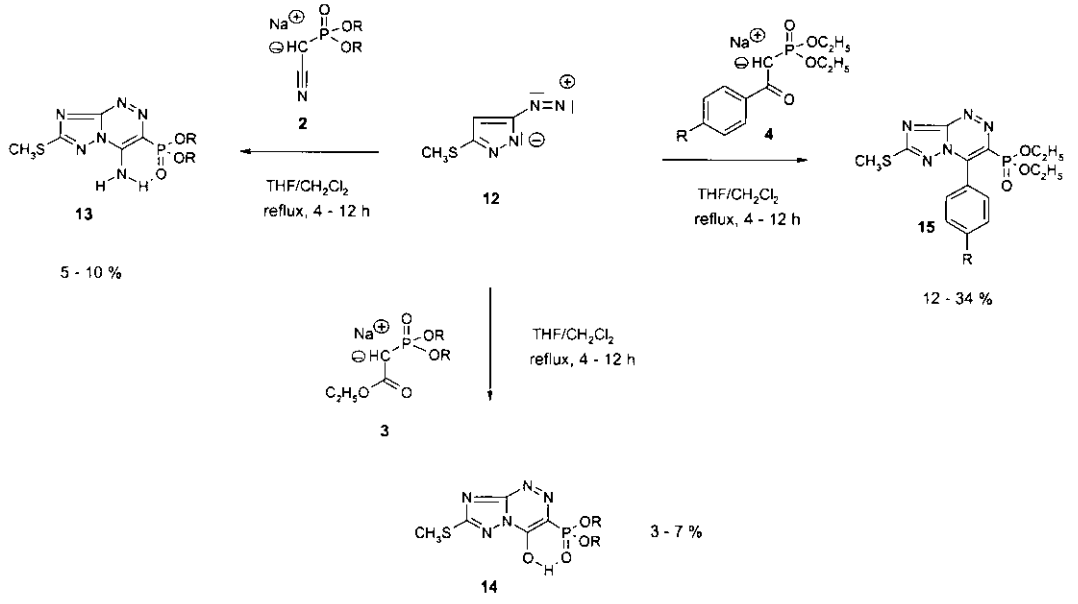


Table 7

13/14	R
a	C_2H_5
b	*i*-C_3H_7

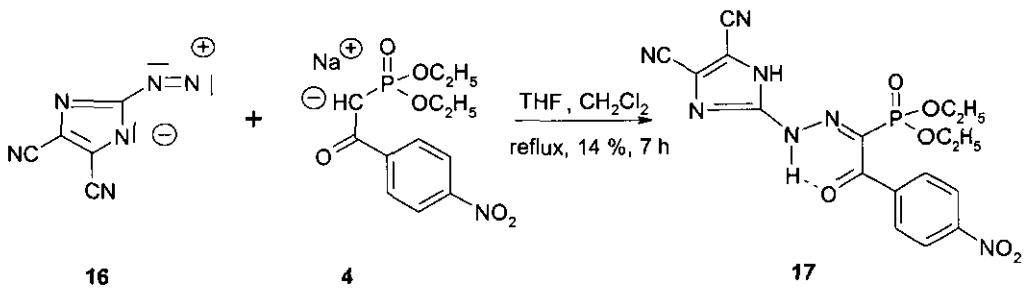
Table 8

15	R
a	H
b	CH_3

This method proved to be efficient and commonly applicable to various heterocyclic structures (indazoles **(1)**, pyrazoles **(8)**, triazoles **(12)**) as well as to diverse phosphonates **(2-4)**. Diazotetrazole did not survive these reaction conditions (decomposition), so that the interesting analogous tetrazolo[3,2-*c*][1,2,4]triazine could not be made.

In one case we succeeded in coupling a 3-diazoimidazole derivative, 3-diazo-4,5-dicyano-imidazole (**16**), with phosphonate **(4)** and isolated the hydrazone **(17)**, which did not cyclize even under strong acidic conditions (Scheme 4).

Scheme 4



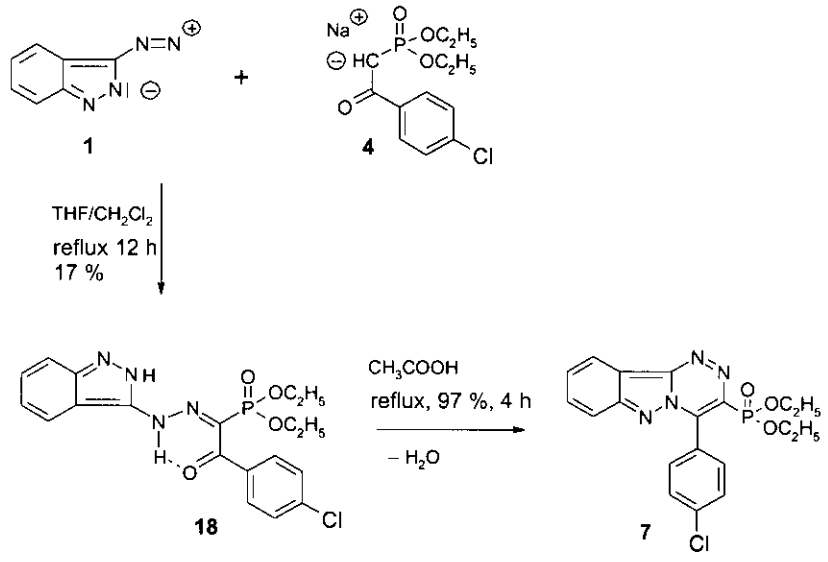
16 **4** **17**

Hydrazone **(18)** was isolable from the reaction of 3-diazoindazole **(1)** with aroylmethylphosphonate **(4)** (Scheme 5). By refluxing in acetic acid this hydrazone **(18)** yielded the expected [1,2,4]triazino[4,3-*b*]indazole **(7)** (Scheme 5).

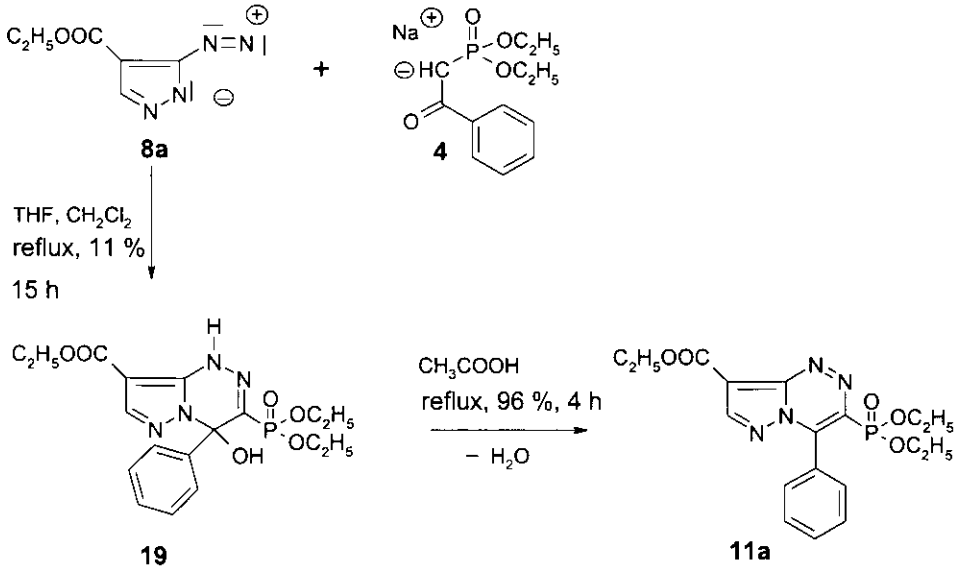
The reaction of 3-diazopyrazol-4-ylcarbonic acid ethyl ester **(8a)** with benzoylmethylphosphonic acid diethyl ester **(4)** yielded in addition to the expected 3-diethylphosphonatopyrazolo[3,2-*c*][1,2,4]triazin-8-ylcarbonic acid ethyl ester **(11a)** the dihydro derivative **(19)** (Scheme 6).

Elimination of water was effected almost quantitatively by heating **11a** in acetic acid (Scheme 6).

Scheme 5



Scheme 6

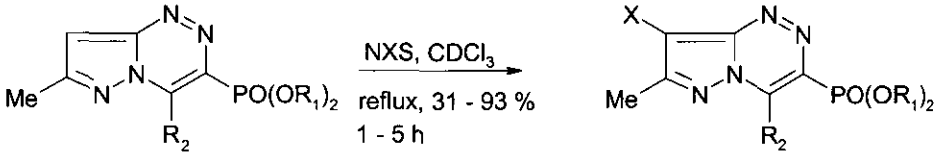


The mechanism of the this reaction may proceed as an initial azocoupling, followed by cyclisation – in the case of phosphonates **(3)** and **(4)** – completed by an elimination of ethanol or water respectively.

The ^{13}C-NMR data of all synthesized new compounds showed characteristic couplings of the phosphorus atom with the adjacent carbon atoms 3 and 4, rangeing from 230 to 235 Hz for C-3 and from 25 to 31 Hz for C-4, depending on the derivative. The signals were detected as dublett. ^{31}P-NMR spectra proved the phosphonato moiety by single peaks with chemical shifts regularly between 8 and 13 ppm.[9] Further NMR-studies showed the molecular structures as 4-amino or 4-hydroxy derivatives respectively, i.e. as bi-/tricyclic 10-/14-π aromatic systems.

The 7-methylpyrazolo[3,2-*c*][1,2,4]triazines **(9c,d;11c-e)** showed high reactivity towards halogenation reactions in position 8 (Scheme 7). Bromination using NBS (1 h, $CHCl_3$, reflux) yielded the 8-bromo derivatives **(20 a,c,d,g)** up to 93 %.[3,10] Iodination using *N*-iodosuccinimide (5 h, $CHCl_3$, reflux) gave up to 75 % of the 8-iodo compounds **(20 b,e,f,h)** (Scheme 7).

Scheme 7



9 c,d; 11c - e **20 a - f**

Table 9

20	R_1	R_2	X
a	C_2H_5	NH_2	Br
b	C_2H_5	NH_2	I
c	C_2H_5	C_6H_5	Br
d	C_2H_5	*p*-Cl-C_6H_4	Br
e	C_2H_5	C_6H_5	I
f	C_2H_5	*p*-NO_2-C_6H_4	I

g	*i*-C_3H_7	NH_2	Br
h	*i*-C_3H_7	NH_2	I

It was also intented to apply the Heck reaction to these halogenated new compounds. The treatment of the iodinated derivatives with bis(triphenylphosphine)palladium-II chloride, triphenylphosphine and copper-I iodide in $(i\text{-Pr})_2NH$ at 70 to 84°C (reflux) enabled coupling with phenylacetylene to give 7-methyl-8-phenylethinylpyrazolo[3,2-*c*][1,2,4]triazin-3-ylphosphonic acid diethyl esters **(21 a – c)**[11] (Scheme 8).

Scheme 8

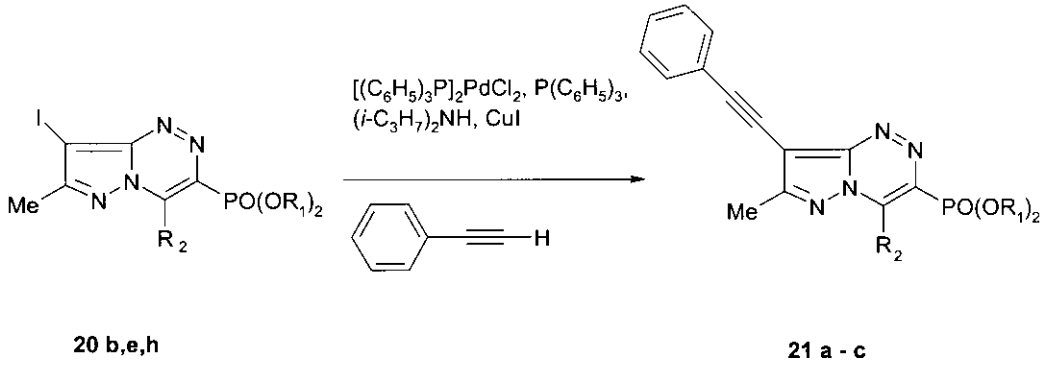


Table 10

21	R_1	R_2
a	C_2H_5	NH_2
b	C_2H_5	C_6H_5
c	*i*-C_3H_7	NH_2

In conclusion, we have shown, that the reaction of heterocyclic diazobetaines with phosphonoacetic acid derivatives **(2)** or aroylmethylphosphonic acid diethyl esters **(4)** is an efficient method for the synthesis of phosphonato substituted azolo[1,2,4]triazines. These are valuable precursors for further reactions, such as halogenation and coupling with phenylacetylene in a modified Heck reaction.

EXPERIMENTAL

All reactions were carried out under argon. $(i\text{-Pr})_2NH$ was freshly distilled from KOH; Et_2O and THF were distilled from Na/benzophenone, CH_2Cl_2 and $CHCl_3$ from CaH_2. Silica gel (60-200 mesh) for column chromatography was obtained from ICN-Biomedicals. Melting points were determined on a Reichert melting point microscope and are uncorrected. UV/VIS spectra were recorded in CH_2Cl_2 on a Hewlett Packard HP 8453A ChemStation and Hewlett Packard HP 8452A diode array spectrophotometer. IR spectra were recorded as KBr pellets on a Perkin Elmer PE 1600 FT-IR spectrophotometer. ^{1}H-NMR spectra were recorded on Bruker WM-250 (at 250.13 MHz) and Varian XL 300 spectrometers (at 299.95 MHz), δ in ppm relative to TMS, J in Hz. ^{13}C-NMR spectra were obtained at 62.89 MHz, 75.43 MHz and 90.56 MHz on the same spectrometers. MS spectra were performed on a Varian MAT-311 A mass spectrometer at 70 eV. Elemental analyses were obtained on a Foss-Heraeus Vario EI.

The syntheses of the phosphonoacetic acid derivates **(2)** and **(3)** as well as the aroylmethylphosphonic acid diethyl esters **(4)** are described in literature.[12] The diazobetaines were synthesized according to the literature[8] starting with the amines, which are commonly available.

Diazo betaines **(1,8,12,16)**: General procedure: 10.0 mmol of the amine were dissolved in a mixture of water (60 mL) and conc. hydrochloric acid (40 mL). After cooling to 0°C an ice-cold solution of 12.0 mmol (0.83 g) of sodium nitrite in water (10 mL) was added dropwise. After 30 min CH_2Cl_2 (80 mL) was added and followed after 10 min by sodium carbonate in small portions with vigorous stirring until pH 7. The organic layer was separated and the aqueous phase extracted with CH_2Cl_2 (3x50 mL). The combined organic layers were dried ($MgSO_4$) and filtered to give *Solution A*.

Phosphonoacetic acid derivates **(2)** and **(3)** and aroylmethylphosphonic acid diethyl esters **(4)**: General procedure:

To 10.0 mmol of the phosphonate in anhydrous THF (40 mL) under argon were added carefully 12.0 mmol (288 mg) of pure NaH. After completion of the hydrogen evolution the mixture was stirred for one more hour under argon: *Solution B*

4-Amino-/4-hydroxy[1,2,4]triazino[4,3-*b*]indazol-3-ylphosphonic acid diethyl esters **(5,6)** and 4-amino-/4-hydroxypyrazolo-/[1,2,4]triazolo[3,2-(c)][1,2,4]triazin-3-ylphosphonic acid diethyl esters **(9,10,13,14)**: General procedure: *Solution A* (200 mL) was added to *Solution B* under argon. The mixture turned dark-red immediately with precipitation of a brownish solid. After 30 min at rt

the mixture was refluxed for 4 to 8 h according to the derivative synthesized. After cooling to rt water (100 mL) was added. The mixture was shaken and then acidified with 6 N hydrochloric acid until the aqueous phase turned yellowbrownish depositing a yellowbrownish precipitate. The aqueous phase was extracted with CH_2Cl_2 (3x80 mL). The combined organic layers were dried ($MgSO_4$), filtered and evaporated yielding a dark-red, oily residue.

4-Amino[1,2,4]triazino[4,3-b]indazol-3-ylphosphonic acid dimethyl ester **(5a)**: After refluxing 10.0 mmol of the above described reaction mixture for 8 h column chromatography (ethyl acetate) and recrystallisation from Et_2O gave pure **5a** as a yellow solid; yield: 620 mg (22%), mp 184-185 °C. UV/VIS (CH_2Cl_2): λ (log ε) = 228 (4.17), 256 (4.34), 368 (4.11), 386*sh* (4.04). IR: ν = 3338*s*/3157*s* (N-H), 2957*m*, 2853*m*, 1613*s*, 1560*m*, 1528*m*, 1440*s*, 1356*s*, 1250*s* /1229*s* (P=O), 1060*s*/1037*s* (P-O-C), 970*m*, 833*s*, 780*s*, 754*s*, 738*m*, 668*m*, 627*m*, 551*s*, 474*s*. ^{1}H-NMR (299.95 MHz, DMSO-d_6): δ = 9.18 (s, 1H, N-H), 8.42 (d, $^3J_{HH}$ = 8.3 Hz, 1H, arom.H), 8.38 (s, 1H, N-H), 7.94 (d, $^3J_{HH}$ = 8.7 Hz, 1H, arom.H), 7.81-7.75 (m, 1H, arom.H), 7.49-7.44 (m, 1H, arom.H), 3.85 (s, 3H, P-O-C$\underline{H}_3$), 3.81 (s, 3H, P-O-C$\underline{H}_3$). ^{13}C-NMR (75.43 MHz, DMSO-d_6): δ = 149.91 (s, C-6a), 142.96 (d, $^2J_{CP}$ = 31.6 Hz, C-4), 130.94 (s, C-8), 122.36 (s, C-10), 120.73 (s, C-9), 118.47 (d, $^1J_{CP}$ = 232.0 Hz, C-3), 112.62 (s, C-10a), 53.70 (d, $^2J_{CP}$ = 5.2 Hz, P-O-$\underline{C}H_3$). ^{31}P-NMR (121.42 MHz, DMSO-d_6): δ = 13.79 (s). EI-MS : m/z (%) = 294 (15, $[M+1]^+$), 293 (100, $[M]^+$), 199 (71), 198 (11), 136 (21), 133 (20), 132 (14), 117 (14), 109 (35), 103 (31), 102 (34), 79 (27), 76 (11), 42 (18), 41 (12) . HR-MS: *m/z* Calcd. $C_{11}H_{12}N_5O_3P$: 293.0677, found: 293.0676. Anal. Calcd for $C_{11}H_{12}N_5O_3P$: C, 45.04; H, 4.13; N, 23.89. Found: C, 45.28; H, 4.05; N, 23.73.

4-Amino[1,2,4]triazino[4,3-b]indazol-3-ylphosphonic acid diethyl ester **(5b)**: After refluxing 10.0 mmol of the above described reaction mixture for 8 h column chromatography (Et_2O/CH_2Cl_2= 1:1) and recrystallisation from the same solvent mixture gave pure **5b** as a yellow solid; yield: 1.6 g (49%), mp 212 °C. UV/VIS (CH_2Cl_2): λ (lg ε) = 228 (4.15), 256 (4.35), 368 (4.14), 380 (4.10). IR (KBr): ν [cm^{-1}] = 3353*m* (NH), 3158*m*, 2983*m*, 2344*w*, 1612*s*, 1527*m*, 1357*m*, 1247s (P=O), 1023*s* (P-O-C), 971*s*, 698*s*. ^{1}H-NMR (299.95 MHz, $CDCl_3$): δ [ppm] = 8.69 (1H, N-H), 8.44 (d, ^{1}H, $^3J_{HH}$ = 8.4 Hz, H-7), 7.80 (d, 1H, $^3J_{HH}$ = 8.7 Hz, H-10), 7.66-7.61 (m, 1H, H-8),

7.55 (1H, N-H), 7.38-7.33 (m, 1H, H-9), 4.47-4.25 (m, 4H, C-O-C$\underline{H}_2$-CH_3), 1.41 (t, 6H, $^3J_{HH}$ = 7.1 Hz, C-O-CH_2-C$\underline{H}_3$). ^{13}C-NMR (75.43 MHz, $CDCl_3$): δ [ppm]= 150.7 (s, C-6a), 143.5 (d, $^4J_{CP}$ = 2.1Hz, C-10b), 142.3 (d, $^2J_{CP}$ = 30.9 Hz, C-4), 131.1 (s, C-8), 122.8 (s, C-10), 121.2 (s, C-9), 119.9 (d, $^1J_{CP}$ = 232.8 Hz, C-3), 116.1 (s, C-7), 113.6 (s, C-10a), 64.2 (d, $^2J_{CP}$ = 6.0 Hz, C-O-$\underline{C}H_2$-CH_3), 16.2 (d, $^3J_{CP}$ = 6.6 Hz, C-O-CH_2-$\underline{C}H_3$). ^{31}P-NMR (121.42 MHz, $CDCl_3$): δ [ppm]= 11.0 (s). EI-MS : m/z (%) = 322 (18, $[M+1]^+$), 321 (100, $M]^+$), 248 (26), 213 (48), 185 (87, $[M-PO(OC_2H_5)_2+H]^+$), 158 (18), 133 (96), 108 (20), 103 (52), 102 (62), 81 (26), 77(8), 76 (19), 65 (19). HR-MS : m/z Calcd for $C_{13}H_{16}N_5O_3P$: 321.0991. Found: 321.0991. Anal. Calcd for $C_{13}H_{16}N_5O_3P$: C, 48.58; H, 5.02; N, 21.85. Found: C, 48.59; H, 4.84; N, 23.73.

4-Amino[1,2,4]triazino[4,3-b]indazol-3-ylphosphonic acid diisopropyl ester **(5c)**: After refluxing 10.0 mmol of the above described reaction mixture for 7.5 h column chromatography (Et_2O/CH_2Cl_2 = 1:1) gave pure **5c** as a yellow solid; yield: 1.32 g (47 %), mp 190 °C. UV/VIS (CH_2Cl_2): λ (log ε) = 228 (4.28), 256 (4.40), 368 (4.19), 388*sh* (4.11). IR (KBr): ν [cm^{-1}] = 3340*m*/ 3161*m*/ 2984*m* (N-H), 1616*s*, 1548*m*, 1441*m*, 1388*m*, 1374*m*, 1357*m*, 1247*s*/1229*s* (P=O), 1177*m*, 1104*m*, 1006*s* (P-O-C), 886*m*, 779*m*, 750*s*, 556*s*. ^{1}H-NMR (299.95 MHz, $CDCl_3$): δ [ppm]= 8.72 (1H, N-H), 8.51-8.48 (m, 1H, arom. C-H), 7.89-7.86 (m, 1H, arom. C-H), 7.74-7.69 (*m*, 1H, *arom.* C-H), 7.45-7.40 (*m*, 1H, *arom.* C-H), 4.93-4.82 (m, 2H, P-O-C$\underline{H}$-$(CH_3)_2$), 1.34 (d, $^3J_{HH}$ = 6.1 Hz, P-O-CH-(C$\underline{H}_3)_2$), 1.34 (d, $^3J_{HH}$ = 6.1 Hz, P-O-CH-(C$\underline{H}_3)_2$). ^{13}C-NMR (62.89 MHz, $CDCl_3$): δ [ppm]= 150.94 (s, C-6a), 143.58 (d, $^4J_{CP}$ = 2.0 Hz, C-10b), 142.00 (d, $^2J_{CP}$= 31.0 Hz, C-4), 131.25 (s, C-8), 122.58 (s, C-10), 121.26 (s, C-9), 120.89 (d, $^1J_{CP}$ = 231.8 Hz, C-3), 116.32 (s, C-7), 113.75 (s, C-10a), 73.27-73.19 (m, P-O-$\underline{C}$H-$(CH_3)_2$), 23.97-23.74 (m, P-O-CH-($\underline{C}H_3)_2$). ^{31}P-NMR (121.42 MHz , $CDCl_3$): δ [ppm]= 9.12 (s). EI-MS : m/z (%) = 350 (7, $[M+1]^+$), 349 (38, $[M]^+$), 307 (10, $[M-C_3H_6]^+$), 266 (13), 265 (100, $[M-2\ C_3H_7O]^+$), 248 (14), 247 (19), 185 (10), 133 (32), 103 (27), 102 (36), 90 (7), 76 (7), 65 (5), 43 (35), 41 (17). HR-MS *m/z* Calcd for $C_{15}H_{20}N_5O_3P$: 349.1305. Found: 349.1306. Anal. Calcd for $C_{15}H_{20}N_5O_3P$: C, 51.56; H, 5.77; N, 20.05. Found: C, 51.34; H, 5.77; N, 20.19. Found: C, 51.34; H, 5.88; N, 20.19.

4-Hydroxy[1,2,4]triazino[4,3-b]indazol-3-ylphosphonic acid diethyl ester **(6a)**: After refluxing 10.0 mmol of the above described reaction mixture for 6.5 h column chromatography (Et_2O/CH_2Cl_2 = 1:1) gave pure **6a** as an orange solid; yield: 688 mg (42%), mp 189-191 °C. UV/VIS (CH_2Cl_2): λ (log ε) = 230 (4.11), 270 (4.36), 280 (4.33), 340*sh* (3.95), 354 (3.98), 402 (3.72). IR (KBr): ν [cm^{-1}] = 3430*w*, 2763*m*, 1700*s*, 1638*m*, 1465*s*, 1259*m* (P=O), 1236*m*, 1052*s*, 1022*s* (P-O-C), 752*s*, 568*s*. ^{1}H-NMR (299.95 MHz, $CDCl_3$): δ [ppm]= 8.42 (d, $^3J_{HH}$ = 8.6 Hz, 1H, arom. H), 7.84 (d, $^3J_{HH}$ = 8.9 Hz, 1H, arom. H), 7.58 (m, 1H, arom. H), 7.28 (t, $^3J_{HH}$ = 7.6 Hz, 1H, arom. H), 4.53-4.37 (m, 4H, P-O-C$\underline{H}_2$-CH_3), 1.46 (t, $^3J_{HH}$ = 7.0 Hz, 6H, P-O-CH_2-C$\underline{H}_3$). ^{13}C-NMR (75.43 MHz, $CDCl_3$): δ [ppm]= 149.86 (s, C-6a), 148.96 (d, $^2J_{CP}$ = 25.2 Hz, C-4), 136.94 (s, C-10b), 131.25 (s, C-8), 127.79 (d, $^1J_{CP}$ = 233.3 Hz, C-3), 123.04 (s, C-10), 121.03 (s, C-9), 117.45 (s, C-7), 107.72 (s, C-10a), 64.54 (d, $^2J_{CP}$ = 6.0 Hz, P-O-$\underline{C}H_2$-CH_3), 16.36 (d, $^3J_{CP}$ = 6.5 Hz, P-O-CH_2-$\underline{C}H_3$). ^{31}P-NMR (121.42 MHz, $CDCl_3$): δ [ppm] = 9.85 (s). EI-MS : m/z (%) = 351 (9, $[M+28+1]^+$), 350 (48, $[M+28]^+$), 322 (12, $[M]^+$), 238 (10), 186 (10), 159 (13), 131 (51), 103 (100), 102 (559, 81 (20), 77 (10), 76 (25), 65 (9). HR-MS m/z Calcd for: $C_{13}H_{15}N_4O_4P$: 322.0832. Found: 322.0833. Anal. Calcd for $C_{13}H_{15}N_4O_4P$: C, 48.44; H, 4.69; N, 17.39. Found: C, 48.63; H, 4.47; N, 17.38.

4-Hydroxy[1,2,4]triazino[4,3-b]indazol-3-ylphosphonic acid diisopropyl ester **(6b)**: After refluxing 10.0 mmol of the above described reaction mixture for 7 h column chromatography (ethyl acetate / ethanol = 10:1) and recrystallisation from ethyl acetate gave pure **6b** as a light brown solid; yield: 450 mg (25 %), mp 202-203 °C. UV/VIS (CH_2Cl_2): λ (log ε) = 228 (4.16), 270 (4.12), 280 (4.05), 352 (4.04), 396 (3.76). IR (KBr): ν [cm^{-1}] = 3389*w*, 2982*s*, 1702*s*, 1638*s*, 1470*s*, 1375*m*, 1242*s* (P=O), 1023*s* (P-O-C), 982*s*, 750*s*. ^{1}H-NMR (250.13 MHz, $CDCl_3$): δ [ppm]= 8.50 (d, 1H, $^3J_{HH}$ = 8.5 Hz, arom. H), 7.88 (d, 1H, $^3J_{HH}$ = 8.9 Hz, arom. H), 7.63-7.57 (m, 1H, arom. H), 7.34-7.28 (m, 1H, arom. H), 5.06-4.94 (m, 2H, P-O-C$\underline{H}$-$(CH_3)_2$), 1.48 (d, 6H, $^3J_{HH}$ = 6.2 Hz, P-O-CH-(C$\underline{H}_3)_2$), 1.41 (d, 6H, $^3J_{HH}$ = 6.2 Hz, P-O-CH-(C$\underline{H}_3)_2$). ^{13}C-NMR (90.56 MHz, $CDCl_3$): δ [ppm]= 150.28 (s, C-6a), 149.01 (d, $^2J_{CP}$ = 25.3 Hz, C-4), 137.40 (s, C-10b), 131.33 (s, C-8), 128.52 (d, $^1J_{CP}$ = 233.46 Hz, C-3), 123.11 (s, C-10), 121.30 (s, C-9),

117.90 (s, C-7), 108.02 (s, C-10a), 73.91 (d, $^2J_{CP}$ = 6.3 Hz, P-O-C<u>H</u>-$(CH_3)_2$), 24.10-24.00 (m, P-O-CH-($C\underline{H}_3$)$_2$). ^{31}P-NMR (121.42 MHz, $CDCl_3$): δ [ppm] = 7.55 (s). EI-MS : m/z (%) = 393 (6, $[M+42+1]^+$), 392 (29, $[M+42]^+$), 350 (12, $[M]^+$), 308 (10, $[M-42]^+$), 267 (14), 266 (100, $[M-2C_3H_7]^+$), 238 (39, $[M-2C_3H_7-N_2]^+$), 159 (12), 141 (18), 123 (29), 103 (66), 102 (32), 99 (14), 76 (11), 43 (88), 42 (36), 41 (70). HR-MS m/z Calcd for $C_{15}H_{19}N_4O_4P$: 350.1145. Found: 350.1146. Anal. Calcd for $C_{15}H_{19}N_4O_4P$: C, 51.41; H, 5.47; N, 16.00. Found: C, 51.54; H, 5.44; N, 15.76.

4-Amino-3-diethylphosphonatopyrazolo[3,2-c][1,2,4]triazin-8-ylcarbonic acid ethyl ester **(9a)**: After refluxing 10.0 mmol of the above described reaction mixture for 12 h column chromatography (ethyl acetate / ethanol = 5:1) and recrystallisation from ethyl acetate gave pure **9a** as a light brown solid; yield: 880 mg (25%), mp 154-155 °C. UV/VIS (CH_2Cl_2): λ (log ε) = 230 (4.21), 294 (3.90), 352 (4.07). IR: ν = 3365*s* (N-H), 3275*m*, 3227*m*, 2984*m*, 1685*s* (C=O), 1629*s*, 1565*s*, 1497*s*, 1440*m*, 1288*m*, 1226*s* (P=O), 1141*m*, 1027*s* (P-O-C), 971*m*, 782*s*, 576*s*, 517*s*. ^{1}H-NMR (250.13 MHz, $CDCl_3$): δ = 8.71 (s, 1H, N-H), 8.62 (s, 1H, H-7), 6.85 (s, 1H, N-H), 4.50 (q, 2H, $^3J_{HH}$ = 7.1 Hz, C-O-C<u>H</u>$_2$-CH_3), 4.37-4.20 (m, 4H, P-O-C<u>H</u>$_2$-CH_3), 1.46 (t, 3H, $^3J_{HH}$ = 7.1 Hz, C-O-CH_2-C<u>H</u>$_3$), 1.40-1.35 (m, 6H, P-O-CH_2-C<u>H</u>$_3$). ^{13}C-NMR (62.89 MHz, $CDCl_3$): δ = 161.91 (s, C=O), 148.47 (s, C-7), 146.74 (s, C-8a), 143.02 (d, $^2J_{CP}$ = 31.1 Hz, C-4), 120.04 (d, $^1J_{CP}$ = 234.6 Hz, C-3), 104.96 (s, C-8), 64.50 (d, $^2J_{CP}$ = 6.2 Hz, P-O-$C\underline{H}_2$-CH_3), 61.08 (s, C-O-$C\underline{H}_2$-CH_3), 16.19 (d, $^3J_{CP}$ = 6.5 Hz, P-O-CH_2-$C\underline{H}_3$), 14.52 (s, C-O-CH_2-$C\underline{H}_3$). ^{31}P-NMR (121.42 MHz, $CDCl_3$): δ = 9.83 (s). EI-MS : m/z (%) = 343 (35, $[M]^+$), 299 (41), 298 (14, $[M-C_2H_5O]^+$), 271 (67), 270 (100, $[M-COOC_2H_5]^+$), 243 (19), 242 (16), 236 (10), 235 (76), 234 (24), 224 (12), 215 (13), 207 (25, $[M-PO(OC_2H_5)_2+H]^+$), 189 (25), 162 (17), 161 (11), 155 (11), 135 (12), 121 (11), 110 (24), 109 (40), 108 (49), 104 (11), 95 (29), 82 (22), 81 (27), 68 (14), 67 (10), 65 (29), 54 (13), 53 (17), 52 (27), 42 (20). HR-MS: m/z Calcd for $C_{12}H_{18}N_5O_5P$: 343.1047, Found: 343.1048. Anal. Calcd for $C_{12}H_{18}N_5O_5P$: C, 41.97; H, 5.29; N, 20.41. Found: C, 41.85; H, 5.24; N, 20.50.

4-Hydroxy-3-diisopropylphosphonatopyrazolo[3,2-c][1,2,4]triazin-8 -ylcarbonic acid ethyl ester

(9b): After refluxing 10.0 mmol of the above described reaction mixture for 6 h column chromatography (Et_2O), followed by treatment with n-hexane in boiling Et_2O and recrystallisation from Et_2O, gave pure **9b** as a white, crystalline solid; yield: 490 mg (13 %), mp 124 °C. UV/VIS (CH_2Cl_2): λ (log ε) = 230 (4.35), 296 (4.00), 352 (4.18). IR (KBr): ν [cm^{-1}] = 3366*m* (N-H), 3275*m*, 3224*m*, 2983*m*, 1692*s* (C=O), 1628*s*, 1566*s*, 1497*m*, 1437*m*, 1386*m*, 1223*m*, 1185*s* (P=O), 1006*m* (P-O-C), 783*m*, 579*m*, 528*m*. ^{1}H-NMR (299.95 MHz, $CDCl_3$): δ [ppm]= 8.84 (s, 1H, N-H), 8.61 (s, 1H, H-7), 6.87 (s, 1H, N-H), 4.87-4.78 (m, 2H, P-O-C$\underline{H}$-$(CH_3)_2$), 4.50 (q, 2H, $^3J_{HH}$ = 7.1 Hz, C-O-C$\underline{H}_2$-CH_3), 1.45 (t, 3H, $^3J_{HH}$ = 7.1 Hz, C-O-CH_2-C$\underline{H}_3$), 1.38 (d, 6H, $^3J_{HH}$ = 6.1 Hz, P-O-CH-(C$\underline{H}_3)_2$), 1.33 (d, 6H, $^3J_{HH}$ = 6.3 Hz, P-O-CH-(C$\underline{H}_3)_2$). ^{13}C-NMR (75.43 MHz, $CDCl_3$): δ [ppm]= 161.70 (s, C=O), 148.16 (s, C-7), 146.52 (d, $^4J_{CP}$ = 2.0 Hz, C-8a), 142.57 (d, $^2J_{CP}$ = 31.3 Hz, C-4), 120.97 (d, $^1J_{CP}$ = 234.8 Hz, C-3), 104.57 (s, C-8), 73.49 (d, $^2J_{CP}$ = 6.5 Hz, P-O-$\underline{C}$H-$(CH_3)_2$), 60.97 (s, C-O-$\underline{C}H_2$-CH_3), 23.94-23.74 (m, P-O-CH-($\underline{C}H_3)_2$), 14.50 (s, C-O-CH_2-$\underline{C}H_3$). ^{31}P-NMR (121.42 MHz, $CDCl_3$): δ [ppm]= 8.01 (s). EI-MS : m/z (%) = 371 (16, $[M]^+$), 314 (11), 313 (42, $[M-C_3H_6O]^+$), 271 (43, $[M-C_3H_6O-C_3H_7]^+$), 270 (32), 242 (13), 216 (22), 215 (100), 108 (12), 95 (10), 42 (35), 40 (13). HR-MS m/z Calcd for $C_{14}H_{22}N_5O_5P$: 371.1357. Found: 371.1355. Anal. Calcd for $C_{14}H_{22}N_5O_5P$: C, 45.27; H, 5.97; N, 18.87. Found: C, 45.24; H, 6.07; N, 18.85.

4-Amino-7-methylpyrazolo[3,2-c][1,2,4]triazin-3-phosphonic acid diethyl ester **(9c)**: After refluxing 10.0 mmol of the above described reaction mixture for 6 h treatment of a CH_2Cl_2 solution of **9c** with Et_2O caused precipitation of crude **9c**. This was purified by recrystallisation from Et_2O as a brown solid; yield:1.86 g (41%), mp 126 °C. UV/VIS (CH_2Cl_2): λ (log ε) = 232 (4.42), 298 (3.88), 344 (3.80). IR: ν = 3336*m* / 3141*s* (N-H), 2983*m*, 1628*s*, 1572*s*, 1390*m*, 1272*m*, 1245*m*, 1213*s* (P=O), 1080*m*, 1040*s* (P-O-C), 973*m*, 959*m*, 799*m*, 751*m*, 657*m*, 627*m*, 579*m*, 518*m*. ^{1}H-NMR (299.95 MHz, $CDCl_3$): δ = 8.43 (s, 1H, N-H), 6.78 (s, 1H, H-8), 6.63 (s, 1H, N-H), 4.37-4.15 (m, 4H, P-O-C$\underline{H}_2$-CH_3), 2.56 (s, 3H, C$\underline{H}_3$ at C-7), 1.37 (dt, 6H, $^3J_{HH}$ = 7.1 Hz, $^4J_{HP}$ = 0.7 Hz, P-O-CH_2-C$\underline{H}_3$). ^{13}C-NMR (75.43 MHz, $CDCl_3$): δ = 156.54 (C-7), 149.39 (d, $^4J_{CP}$ = 2.0 Hz, C-8a), 142.57 (d, $^2J_{CP}$ = 31.0 Hz, C-4), 115.66 (d, $^1J_{CP}$ = 236.9 Hz, C-3),

97.97 (s, C-8), 63.73 (d, $^2J_{CP}$ = 5.9 Hz, P-O-$\underline{C}H_2$-CH_3), 16.20 (d, $^3J_{CP}$ = 6.8 Hz, P-O-CH_2-$\underline{C}H_3$), 14.54 (s, $\underline{C}H_3$ at C-7). ^{31}P-NMR (121.42 MHz, $CDCl_3$): δ = 12.65 (s). EI-MS : m/z (%) = 285 ($[M]^+$), 241 (30), 213 (13), 212 (100), 177 (91), 176 (35), 149 (69), 148 (13), 122 (19), 109 (21), 108 (21), 97 (54), 82 (20), 81 (28), 67 (14), 66 (27), 65 (16), 55 (11), 54 (22), 53 (13), 45 (61), 43 (18), 42 (16), 41 (28). HR-MS: *m/z* Calcd for $C_{10}H_{16}N_5O_3P$: 285.0991. Found: 285.0991. Anal. Calcd for $C_{10}H_{16}N_5O_3P$: C, 42.09; H, 5.66; N, 24.56. Found: C, 41.96; H, 5.87; N, 24.61.

3-Diethylphosphonato-4-hydroxypyrazolo[3,2-c][1,2,4]triazin-8-ylcarbonic acid ethyl ester **(10)**: Refluxing 10.0 mmol of the above described reaction mixture for 2 h followed by treatment of a solution of **10** in CH_2Cl_2 with n-hexane gave pure **10** as a yellow solid; yield: 1.61 g (46 %), mp 140 °C. UV/VIS (CH_2Cl_2): λ (log ε) = 230 (4.03), 260 (4.36), 330 (4.25). IR (KBr): ν [cm^{-1}] = 3001*m*, 1731*s*, 1709*s*, 1600*s*, 1517*s*, 1242*s* (P=O), 1128*s*, 1022*s* (P-O-C), 776*m*. ^{1}H-NMR (250.13 MHz, $CDCl_3$): δ [ppm]= 8.28 (s, H-7), 4.44-4.32 (m, 6H, C-O-C$\underline{H}_2$-CH_3, P-O-C$\underline{H}_2$-CH_3), 1.42-1.37 (m, 9H, C-O-CH_2-C$\underline{H}_3$, P-O-CH_2-C$\underline{H}_3$). ^{13}C-NMR (62.89 MHz, $CDCl_3$): δ [ppm] = 161.71 (s, C=O), 147.78 (d, $^2J_{CP}$ = 24.6 Hz, C-4), 144.91 (s, C-7), 143.44 (s, C-8a), 134.91 (d, $^1J_{CP}$ = 234.8 Hz, C-3), 98.60 (s, C-8), 64.51 (d, $^2J_{CP}$ = 6.2 Hz, P-O-$\underline{C}H_2$-CH_3), 61.36 (s, C-O-$\underline{C}H_2$-CH_3), 16.40 (d, $^3J_{CP}$ = 6.2 Hz, P-O-CH_2-$\underline{C}H_3$), 14.41 (s, C-O-CH_2-$\underline{C}H_3$). ^{31}P-NMR (121.42 MHz, $CDCl_3$): δ [ppm] = 5.35 (s). EI-MS : m/z (%) = 372 (26, $[M+28]^+$), 344 (29, $M]^+$), 299 (17, $[M-C_2H_5O]^+$), 298 (33, $[M-C_2H_6O]^+$), 271 (16), 264 (20), 263 (59), 236 (37), 235 (47), 190 (56), 189 (79), 163 (22), 162 (29, $[M-C_2H_6O$-$PO(OC_2H_5)_2+H]^+$), 152 (23), 136 (47), 135 (100), 134 (43), 109 (70), 108 (44), 81(73), 68 (13), 65 (28), 52 (59). HR-MS m/z Calcd for $C_{12}H_{17}N_4O_6P$: 344.0887. Found: 344.0888. Anal. Calcd for $C_{12}H_{17}N_4O_6P$: C, 41.85; H, 4.98; N, 16.28. Found: C, 41.71; H, 5.03; N, 15.99.

4-Amino-7-methylmercapto[1,2,4]triazolo[3,2-c][1,2,4]triazin-3-ylphosphonic acid diethyl ester **(13a)**: After refluxing 10.0 mmol for 7.5 h column chromatography (ethyl acetate) and recrystallisation from ethyl acetate gave pure **13a** as light brown needles; yield: 315 mg (9%), mp 143-145 °C. UV/VIS (CH_2Cl_2): λ (log ε) = 228 (3.67), 254 (3.96), 308 (3.34). IR: ν =

3421*m*, 2772*s*, 1724*m*, 1616*s*, 1507*s*, 1430*m*, 1376*m*, 1274*s*, 1237*s* (P=O), 1208*m*, 1160*m*, 1074*s*, 1021*s* (P-O-C), 758*m*, 533*m*. ^{1}H-NMR (299.95 MHz, $CDCl_3$): δ = 8.70 (s, 1H, N-H), 6.81 (s, 1H, N-H), 4.37-4.21 (m, 4H, P-O-C$\underline{H}_2$-CH_3), 2.75 (s, 3H, S-CH_3), 1.38 (dt, 6H, $^{3}J_{HH}$ = 7.1 Hz, $^{4}J_{HP}$ = 0.8 Hz, P-O-CH_2-C$\underline{H}_3$). ^{13}C-NMR (75.43 MHz, $CDCl_3$): δ = 171.16 (s, C-7), 155.50 (d, $^{4}J_{CP}$ = 1.9 Hz, C-8a), 142.22 (d, $^{3}J_{CP}$ = 32.1 Hz, C-4), 121.68 (d, $^{2}J_{CP}$ = 235.2 Hz, C-3), 64.44 (d, $^{2}J_{CP}$ = 6.2 Hz, P-O-$\underline{C}H_2$-CH_3), 16.17 (d, $^{3}J_{CP}$ = 6.5 Hz, P-O-CH_2-$\underline{C}H_3$), 14.10 (s, S-$\underline{C}H_3$). ^{31}P-NMR (121.42 MHz, $CDCl_3$): δ = 9.69 (s). EI-MS : m/z (%) = 318 (20, $[M]^+$), 274 (73), 246 (13), 245 (96), 211 (12), 210 (100), 209 (16), 199 (13), 182 (25, $[M-PO(OC_2H_5)_2+H]^+$), 130 (41), 121 (11), 114 (16), 109 (13), 108 (29), 99 (23), 97 (15), 85 (20), 82 (25), 81 (42), 74 (17), 68 (25), 65 (27), 54 (10), 53 (10), 47 (20), 43 (11), 41 (16). HR-MS: m/z Calcd for $C_9H_{15}N_6O_3PS$: 318.0064. Found: 318.0064. Anal. Calcd for $C_9H_{15}N_6O_3PS$: C, 33.96; H, 4.75; N, 26.42; S, 10.05. Found: C, 34.01; H, 4.71; N, 26.35; S, 9.94.

4-Amino-7-methylmercapto[1,2,4]triazolo[3,2-c][1,2,4]triazin-3-ylphosphonic acid diisopropyl ester **(13b)**: After refluxing 10.0 mmol of the above described reaction mixture for 7 h column chromatography (ethyl acetate / Et_2O = 5:2), stirring in Et_2O for 24 h and recrystallisation from Et_2O gave pure **13b** as a light brown solid; yield: 180 mg (5 %), mp 124 °C. UV/VIS (CH_2Cl_2): λ (log ε) = 230*sh* (3.82), 254 (4.42), 318 (3.83). IR (KBr): ν [cm^{-1}] = 3080*s*, 2908*s*, 2750*s*, 1629*s*, 1523*m*, 1450*s*, 1288*s* (P=O), 1102*w*, 1030*s* (P-O-C), 999*s*, 857*w*, 709*s*, 581*w*. ^{1}H-NMR (299.95 MHz, acetone-d_6): δ [ppm]= 8.80 (s, 1H, N-H), 8.31 (s, 1H, N-H), 4.89-4.76 (m, 2H, P-O-C$\underline{H}$-$(CH_3)_2$), 2.72 (s, 3H, S-C$\underline{H}_3$), 1.36 (d, 6H, $^{3}J_{HH}$ = 6.2 Hz, P-O-CH-(C$\underline{H}_3)_2$), 1.28 (d, 6H, $^{3}J_{HH}$ = 6.1 Hz, P-O-CH-(C$\underline{H}_3)_2$). ^{13}C-NMR (62.89 MHz, acetone-d_6): δ [ppm]= 170.67 (s, C-7), 157.01 (s, C-8a), 144.20 (d, $^{2}J_{CP}$ = 33.8 Hz, C-4), 123.73 (d, $^{1}J_{CP}$ = 234.3 Hz, C-3), 73.32 (d, $^{2}J_{CP}$ = 5.2 Hz, P-O-$\underline{C}$H-$(CH_3)_2$), 24.14-23.87 (m, P-O-CH-($\underline{C}H_3)_2$), 13.90 (s, S-$\underline{C}H_3$). ^{31}P-NMR (121.42 MHz, acetone-d_6): δ [ppm]= 7.23 (s). EI-MS : m/z (%) = 347 (5, $[M+1]^+$), 346 (33, $[M]^+$), 289 (19), 288 (73, $[M-C_3H_6O]^+$), 263 (15), 262 (27), 247 (11), 246 (100), 245 (53), 217 (18), 199 (12), 182 (17), 155 (15), 130 (22), 115 (43), 99 (21), 82 (14), 74 (15), 68 (15), 43 (71), 42 (10), 41 (23). HR-MS m/z Calcd for $C_{11}H_{19}N_6O_3PS$: 346.0977. Found: 346.0977.

Anal. Calcd for $C_{11}H_{19}N_6O_3PS$: C, 38.14; H, 5.53; N, 24.28; S, 9.24. Found: C, 38.11; H, 5.22; N, 24.04; S, 9.12.

4-Hydroxy-7-methylmercapto[1,2,4]triazolo[3,2-c][1,2,4]triazin-3-ylphosphonic acid diethyl ester **(14a)**: After refluxing 10.0 mmol of the above described reaction mixture for 7.5 h column chromatography (ethyl acetate) and two recrystallisations from the same solvent with activated carbon gave pure **14a** as a light brown solid; yield: 235 mg (7 %), mp 164-165 °C. UV/VIS (CH_2Cl_2): λ (log ε) = 236 (4.29), 312 (3.82). IR (KBr): ν [cm^{-1}] = 3420*m* (O-H), 3231*w*, 3126*w*, 2982*s* / 2930*s* (S-CH_3), 2772*s*, 1724*s*, 1610*s*, 1507*s*, 1376*m*, 1273*s* (P=O), 1237*s*, 1209*m*, 1161*m*, 1073*s* (P-O-C), 1021*s*, 985*m*, 933*m*, 758*s*, 553*s*, 481*m*. ^{1}H-NMR (299.95 MHz, $CDCl_3$): δ [ppm]= 4.46-4.29 (m, 4H, P-O-C$\underline{H}_2$-CH_3), 2.69 (s, 3H, S-C$\underline{H}_3$), 1.40 (dt, 6H, $^3J_{HH}$ = 7.1 Hz, $^4J_{HP}$ = 0.7 Hz, P-O-CH_2-C$\underline{H}_3$). ^{13}C-NMR (75.43 MHz, $CDCl_3$): δ [ppm]= 168.27 (s, C-7), 151.31 (s, C-8a), 146.91 (d, $^2J_{CP}$ = 26.1 Hz, C-4), 133.13 (d, $^1J_{CP}$ = 234.6 Hz, C-3), 64.86 (d, $^2J_{CP}$ = 6.5 Hz, P-O-$\underline{C}H_2$-CH_3), 16.28 (d, $^3J_{CP}$ = 6.5 Hz, P-O-CH_2-$\underline{C}H_3$), 14.05 (s, S-$\underline{C}H_3$). ^{31}P-NMR (121.42 MHz, $CDCl_3$): δ [ppm]= 6.60 (s). EI-MS : m/z (%) = 348 (10, $[M+28+1]^+$), 347 (64, $[M+28]^+$), 320 (6, $[M+1]^+$), 319 (45, $[M]^+$), 274 (14), 246 (18), 239(58), 238 (94), 211 (24), 210 (33), 192 (13), 183 (38), 164 (25), 157 (19), 156 (21), 155 (20), 141 (11), 136 (12), 128 (15), 113 (46), 109 (36), 108 (37), 99 (17), 85 (100), 81 (52), 74 (20), 73 (20), 69 (18), 68 (16), 65 (16), 47 (23), 43 (11). HR-MS: m/z Calcd for $C_9H_{14}N_5O_4PS$: 319.0503. Found: 319.0502. Anal. Calcd for $C_9H_{14}N_5O_4PS$: C, 33.85; H, 4.42; N, 21.94; S, 10.02. Found: C, 38.11; H, 5.22; N, 20.09; S, 10.12.

4-Hydroxy-7-methylmercapto[1,2,4]triazolo[3,2-c][1,2,4]triazin-3-ylphosphonic acid diisopropyl ester **(14b)**: After refluxing 10.0 mmol of the above described reaction mixture for 7 h column chromatography (ethyl acetate) and recrystallisation from the same solvent with addition of activated carbon gave pure **14b** as a brown solid; yield: 85 mg (2 %), mp 126 °C. UV/VIS (CH_2Cl_2): λ (log ε) = 238 (4.31), 310 (3.87). IR (KBr): ν [cm^{-1}] = 3420*m*, 2981*s* (O-H), 2932*m*, 2747*m*, 1729*s*, 1599*s*, 1510*s*, 1435*s*, 1375*s*, 1269*s*, 1236*s* (P=O), 1207*m*, 1168*m*, 1100*m*, 1002*s* (P-O-C), 934*m*, 888*m*, 767*m*, 603*m*, 568*s*. ^{1}H-NMR (299.95 MHz, acetone-d_6): δ [ppm] = 4.73 (q, 2H, $^3J_{HH}$ = 6.4 Hz, P-O-C$\underline{H}$-$(CH_3)_2$), 2.67 (s, 3H, S-C$\underline{H}_3$), 1.18 (m, 12H, P-O-CH-

$(CH_3)_2$). ^{13}C-NMR (75.43 MHz, acetone-d_6): δ [ppm]= 167.67 (s, C-7), 157.85 (s, C-8a), 151.06 (d, $^2J_{CP}$ = 29.6 Hz, C-4), 131.39 (d, $^1J_{CP}$ = 235.1 Hz, C-3), 73.03 (d, $^2J_{CP}$ = 5.0 Hz, P-O-CH-$(CH_3)_2$), 24.12-23.79 (m, P-O-CH-$(CH_3)_2$), 14.01 (s, S-CH_3). ^{31}P-NMR (121.42 MHz, acetone-d_6): δ [ppm]= 4.67 (s). EI-MS : m/z (%) = 389 (7, $[M+42]^+$), 348 (8, $[M+1]^+$), 347 (47, $[M]^+$), 290 (24), 289 (14), 264 (36), 263 (29), 247 (14), 246 (29), 225 (20), 224 (16), 197 (20), 155 (26), 149 (22), 130 (18), 128 (19), 123 (12), 108 (19), 99 (15), 85 (32), 74 (13), 43 (86), 42 (68), 41 (100). HR-MS: m/z Calcd for $C_{11}H_{18}N_5O_4PS$: 347.0817. Found: 347.0817. Anal. Calcd for $C_{11}H_{18}N_5O_4PS$: C, 38.03; H, 5.23; N, 20.17; S, 8.92. Found: C, 38.11; H, 5.22; N, 20.09; S, 8.84.

4-Aryl[1,2,4]triazino[4,3-*b*]indazol-3-ylphosphonic acid diethyl esters **(7),** 4-arylpyrazolo[3,2-*c*][1,2,4]triazin-3-ylphosphonic acid diethyl esters **(11)** and 4-aryl[1,2,4]triazolo[3,2-*c*][1,2,4]triazin-3-ylphosphonic acid diethyl esters **(15)**: General procedure: As described above the reaction mixture (*Solution A* plus *B*) was refluxed for 12 h. After cooling to rt water (50 mL) was added. The mixture was shaken and the organic layer was separated, dried ($MgSO_4$), filtered and evaporated yielding a brown, oily residue.

4-Phenyl[1,2,4]triazino[4,3-b]indazol-3-ylphosphonic acid diethyl ester **(7a)**: After refluxing 10.0 mmol of the above described reaction mixture for 12 h column chromatography (ethyl acetate / n-hexane = 5:1) and recrystallisation from Et_2O gave pure **7a** as an orange solid; yield: 85 mg (2 %), mp 146-147 °C. UV/VIS (CH_2Cl_2): λ (log ε) = 230 (4.28), 242 (4.18), 282 (4.47), 352 (3.74), 366 (3.75), 422 (3.43). IR (KBr): ν [cm^{-1}] = 3448*m*, 3057*w*, 2979*w*, 1631*m*, 1507*w*, 1468*m*, 1445*m*, 1350*m*, 1295*m*, 1262*s* (P=O), 1202*m*, 1170*m*, 1054*m*, 1025*s* (P-O-C), 979*m*, 771*m*, 697*m*, 645*m*, 580*m*, 546*m*, 508*m*. ^{1}H-NMR (299.95 MHz, $CDCl_3$): δ [ppm]= 7.85-6.76 (m, 9H, arom. C-H), 4.38-4.29 (m, 4H, P-O-CH_2-CH_3), 1.39 (t, 6H, $^3J_{HH}$ = 6.9 Hz, P-O-CH_2-CH_3). ^{13}C-NMR (90.56 MHz, $CDCl_3$): δ [ppm]= 151.71 (s, C-6a), 145.97 (s, C-10b), 139.46 (d, $^1J_{CP}$ = 233.4 Hz, C-3), 137.26 (d, $^2J_{CP}$ = 29.5 Hz, C-4), 131.87 (s, arom. C-H), 131.41 (s, arom. C-H), 130.27 (s, arom. C-H), 128.62 (s, arom. C-H), 127.63 (s, C-1′), 124.64 (s, C-10), 121.24 (s, C-9), 117.53 (s, C-7), 114.12 (s, C-10a), 63.89 (d, $^2J_{CP}$ = 6.4 Hz, P-O-CH_2-CH_3), 16.17 (d, $^3J_{CP}$ = 6.9 Hz, P-O-CH_2-CH_3). EI-MS : m/z (%) = 383 (24, $[M+1]^+$), 382 (100, $[M]^+$), 367 (17),

338 (21), 337 (15, $[M-C_2H_5O]^+$), 309 (20), 274 (41), 273 (59), 247 (19), 246 (77), 245 (60, $[M-PO(OC_2H_5)_2]^+$), 220 (17), 219 (99), 218 (11), 163 (12), 144(18), 118 (10), 117 (21), 116 (92), 115 (11), 103 (15), 102 (55), 90 (18), 89 (31), 81(17), 77(11), 65 (13), 51 (7). HR-MS: m/z Calcd for $C_{19}H_{19}N_4O_3P$: 382.1194. Found: 382.1193. Anal. Calcd for $C_{19}H_{19}N_4O_3P$: C, 59.68; H, 5.01; N, 14.65. Found: C, 59.57; H, 5.02; N, 14.49.

4-(4-Chlorophenyl)-[1,2,4]triazino[4,3-b]indazol-3-ylphosphonic acid diethyl ester **(7b)**: After refluxing 10.0 mmol of the above described reaction mixture for 12 h column chromatography (ethyl acetate / n- hexane = 1:1) and recrystallisation from Et_2O gave pure **7b** *as an orange* solid; yield: 60 mg (1 %). Alternatively **7b** could be synthesized by refluxing 1 mmol of **18** in acetic acid (10 mL) for 7 h, diluting with water and neutralising by addition of sodium carbonate followed by extraction with $CHCl_3$; yield: 408 mg (98 %), mp 146-147 °C. UV/VIS (CH_2Cl_2): λ (log ε) = 230 (4.36), 282 (4.52), 352 (3.83), 364 (3.86), 426 (3.57). IR: ν = 2981*m*, 1628*m*, 1598*m*, 1472*s*, 1396*m*, 1350*m*, 1295*s*, 1261*s* (P=O), 1200*m*, 1171*m*, 1092*m*, 1031*s* (P-O-C), 983*s*, 955*m*, 834*m*, 763*s*, 544*m*, 518*m*. ^{1}H-NMR (250.13 MHz, $CDCl_3$): δ = 8.68-8.64 (m, 1H, arom. H), 7.98-7.57 (m, 7H, arom. H), 4.30-4.13 (m, 4H, P-O-C$\underline{H}_2$-CH_3), 1.31-1.26 (m, 6H, P-O-CH_2-C$\underline{H}_3$). ^{13}C-NMR (62.89 MHz, $CDCl_3$): δ = 151.73 (s, C-6a), 145.98 (d, $^4J_{CP}$ = 3.1 Hz, C-10b), 139.40 (d, $^1J_{CP}$ = 233.1 Hz, C-3), 137.86 (s, C-4´), 136.74 (d, $^2J_{CP}$ = 38.4 Hz, C-4), 132.04 (s, arom. C), 131.87 (s, arom. C), 129.01 (s, C-10), 125.99 (s, C-1´), 124.83 (s, C-9), 121.27 (s, C-8), 117.50 (s, C-7), 114.20 (s, C-10a), 64.01 (d, $^2J_{CP}$ = 6.9 Hz, P-O-$\underline{C}H_2$-CH_3), 16.20 (d, $^3J_{CP}$ = 7.0 Hz, P-O-CH_2-$\underline{C}H_3$). EI-MS : m/z (%) = 418 (20, $[M+2]^+$), 417 (14), 416 (55, $[M]^+$), 401 (11), 372 (11), 343 (15), 309 (17), 308 (29), 307 (31), 282 (17),281 (14), 280 (51), 279 (15), 273 (25), 255 (20), 254 (11), 253 (67), 245 (16), 144 (14), 136 (18), 117 (22), 116 (100), 102 (53), 90 (11), 89 (19), 81 (22), 65 (16). HR-MS: m/z Calcd for $C_{19}H_{18}N_4O_3ClP$: 416.0803. Found: 416.0801. Anal. Calcd for $C_{19}H_{18}N_4O_3ClP$: C, 54.75; H, 4.35; N, 13.44. Found: C, 54.77; H, 4.31; N, 13.52.

3-Diethylphosphonato-4-phenylpyrazolo[3,2-c][1,2,4]triazin-8-ylcarbonic acid ethyl ester **(11a)**: After refluxing 10.0 mmol of the above described reaction mixture for 6 h column chromatography (ethyl acetate) and recrystallisation from Et_2O gave pure **11a** as as yellow solid; yield: 290 mg (7 %), mp 104 °C. Alternatively **11a** could be synthesized by refluxing 1.0

mmol of **19** in acetic acid (20 mL), diluting with water and neutralising by addition of sodium carbonate followed by extraction with $CHCl_3$; yield: 390 mg (96 %), mp 104 °C. UV/VIS (CH_2Cl_2): λ (log ε) = 232sh (4.17), 248 (4.30), 296 (3.73), 308*sh* (3.70), 356 (3.61), 390*sh* (3.52). IR: ν = 3431*m*, 2979*m*, 1726*s* (C=O), 1576*s*, 1476*s*, 1340*s*, 1273*s*, 1201*s* (P=O), 1142*s*, 1051*s*/1019*s* (P-O-C), 982*m*, 751*m*, 702*m*, 531*s*. ^{1}H-NMR (299.95 MHz, $CDCl_3$): δ = 8.72 (s, 1H, H-7), 7.81-7.63 (m, 5H, arom. H), 4.55 (q, 2H, $^3J_{HH}$ = 7.1 Hz, C-O-C$\underline{H}_2$-CH_3), 4.31-4.07 (m, 4H, P-O-C$\underline{H}_2$-CH_3), 1.48 (t, 3H, $^3J_{HH}$ = 7.1 Hz, C-O-CH_2-C$\underline{H}_3$), 1.22 (t, 6H, $^3J_{HH}$ = 7.1 Hz, P-O-CH_2-C$\underline{H}_3$). ^{13}C-NMR (90.56 MHz, $CDCl_3$): δ = 161.36 (s, C=O), 149.45 (s, C-7), 147.78 (s, C-8a), 140.03 (d, $^2J_{CP}$ = 28.9 Hz, C-4), 138.15 (d, $^1J_{CP}$ = 235.0 Hz, C-3), 131.94, (s, C-4´), 130.11 (s, arom. C), 128.57 (s, arom. C), 126.23 (s, C-1´), 106.24 (s, C-8), 64.04 (d, $^2J_{CP}$ = 6.3 Hz, P-O-$\underline{C}H_2$-CH_3), 61.38 (s, C-O-$\underline{C}H_2$-CH_3), 16.14 (d, $^3J_{CP}$ = 6.7 Hz, P-O-CH_2-$\underline{C}H_3$), 14.51 (s, C-O-CH_2-$\underline{C}H_3$). ^{31}P-NMR (121.42 MHz, $CDCl_3$): δ = 7.86 (s) EI-MS : m/z (%) = 406 (3), 405 (20, $[M+1]^+$), 404 (100, $[M]^+$), 375 (11, $[M-C_2H_5]^+$), 360 (37), 359 (35, $[M-C_2H_5O]^+$), 358 (29), 331 (33, $[M-COOC_2H_5]^+$), 296 (16), 295 (32), 286 (12), 285 (12), 250 (17), 249 (11), 223 (13), 222 (35), 221 (37), 196 (16), 195 (27), 194 (20), 165 (12), 129 (12), 110 (11), 105 (15), 104 (42), 103 (24), 102 (51), 89 (19), 81 (26), 77 (18), 65 (19), 52 (9). HR-MS: m/z Calcd for $C_{18}H_{21}N_4O_5P$: 404.1248. Found: 404.1246. Anal. Calcd for $C_{18}H_{21}N_4O_5P$: C, 53.45; H, 5.24; N, 13.86. Found: C, 53.37; H, 5.45; N, 13.87.

3-Diethylphosphonato-4-(4´-methylphenyl)pyrazolo[3,2-c][1,2,4]triazin-8-ylcarbonic acid ethyl ester **(11b)***:* After refluxing 10.0 mmol of the above described reaction mixture for 15 h column chromatography (ethyl acetate / ethanol = 10:1) and recrystallisation from Et_2O gave pure **11b** as a yellow solid; yield: 210 mg (5 %), mp 130 °C. UV/VIS (CH_2Cl_2): λ (log ε) = 232sh (4.38), 248 (4.45), 298 (3.89), 358 (3.77), 378*sh* (3.75). IR (KBr): ν [cm^{-1}] = 3447*m*, 2988*m* (arom. H), 1703*s* (C=O), 1611*w*, 1566*m*, 1522*m*, 1487*s*, 1436*m*, 1373*w*, 1276*s*, 1252*s*/1207*s* (P=O), 1140*s*, 1052*s*/1022*s* (P-O-C), 939*m*, 786k, 753*m*, 589*s*, 552*s*, 459*w*. ^{1}H-NMR (250.13 MHz, $CDCl_3$): δ [ppm] = 8.71 (s, 1H, H-7), 7.70 (d, 2H, $^3J_{HH}$ = 8.0 Hz, C-H), 7.43 (d, 2H, $^3J_{HH}$ = 8.0 Hz, C-H), 4.54 (q, 2H, $^3J_{HH}$ = 7.1 Hz, C-O-C$\underline{H}_2$-CH_3), 4.29-4.13 (m, 4H, P-O-C$\underline{H}_2$-CH_3), 2.49 (s, 3H, C_6H_4-CH_3), 1.48 (t, 3H, $^3J_{HH}$ = 7.1 Hz, C-O-CH_2-C$\underline{H}_3$), 1.24 (t, 6H, $^3J_{HH}$ = 7.0 Hz, P-

O-CH_2-C$\underline{H}_3$). ^{13}C-NMR (62.89 MHz, $CDCl_3$): δ [ppm]= 161.40 (s, C=O), 149.39 (s, C-7), 147.80 (s, C-8a), 142.68 (s, C-4´), 140.43 (d, $^2J_{CP}$ = 30.9 Hz, C-4), 138.04 (d, $^1J_{CP}$ = 236.4 Hz, C-3), 130.14 (s, arom. C), 129.27 (s, arom. C), 123.20 (s, C-1´), 106.15 (s, C-8), 64.02 (d, $^2J_{CP}$ = 7.0 Hz, P-O-$\underline{C}H_2$-CH_3), 61.34 (s, C-O-$\underline{C}H_2$-CH_3), 21.76 (s, arom. CH_3), 16.14 (d, $^3J_{CP}$ = 6.3 Hz, P-O-CH_2-$\underline{C}H_3$), 14.51 (s, C-O-CH_2-$\underline{C}H_3$). ^{31}P-NMR (121.42 MHz, $CDCl_3$): δ [ppm]= 19.37 (s). EI-MS : m/z (%) = 420 (4), 419 (22, $[M+1]^+$), 418 (100, $[M]^+$), 374 (15), 373 (22, $[M-C_2H_5O]^+$), 372 (26), 359 (52), 345 (22, $[M-COOC_2H_5]^+$), 331 (16), 310 (12), 309 (31), 295 (21), 236 (11), 235 (14), 221 (25), 209 (18), 298 (12), 158 (9), 119(11), 118 (22), 117 (22), 115 (22), 103 (11), 91 (14), 81 (5), 65 (15). HR-MS: m/z Calcd for $C_{19}H_{23}N_4O_5P$: 418.1407. Found: 418.1408. Anal. Calcd for $C_{19}H_{23}N_4O_5P$: C, 54.53; H, 5.54; N, 13.40. Found: C, 54.52; H, 5,64; N, 13.51.

7-Methyl-4-phenylpyrazolo[3,2-c][1,2,4]triazin-3-ylphosphonic acid diethyl ester (**11c**): After refluxing 10.0 mmol of the above described reaction mixture for 5.5 h column chromatography (*ethyl acetate / n- hexane* = 10:3) and recrystallisation from Et_2O gave pure **11c** as a yellow solid; yield: 2.17 g (41 %), mp 120-121 °C. UV/VIS (CH_2Cl_2): λ (log ε) = 244 (4.44), 286*sh* (3.74), 366 (3.50). IR (KBr): ν [cm^{-1}] = 3419*s*, 2986*m*, 1558*m*, 1514*w*, 1468*s*, 1444*w*, 1286*m*, 1244*s* (P=O), 1217*m*, 1161*m*, 1057*s*, 1025*s* (P-O-C), 983*m*, 952*m*, 776*m*, 750*m*, 693*s*, 585*s*, 510*m*, 453*m*. ^{1}H-NMR (250.13 MHz, $CDCl_3$): δ [*ppm*]= 7.79-7.75 (m, 2H, H-2´, H-6´), 7.68-7.59 (m, 3H, H-3´, H-4´, H-5´), 7.13 (s, 1H, H-8), 4.29-4.05 (m, 4H, P-O-$C\underline{H}_2$-CH_3), 2.56 (s, 3H, $C\underline{H}_3$), 1.21 (t, 6H, $^3J_{HH}$ = 7.1 Hz, P-O-CH_2-$C\underline{H}_3$). ^{13}C-NMR (90.56 MHz, $CDCl_3$): δ [ppm] = 158.44 (s, C-7), 151.06 (s, C-8a), 139.19 (d, $^2J_{CP}$ = 35.2 Hz, C-4), 134.90 (d, $^1J_{CP}$ = 239.1 Hz, C-3), 131.37 (s, arom. C), 130.03 (s, arom. C), 128.40 (s, arom. C), 127.19 (s, C-1´), 99.32 (s, C-8), 63.54 (d, $^2J_{CP}$ = 6.5 Hz, P-O-$\underline{C}H_2$-CH_3), 16.14 (d, $^3J_{CP}$ = 6.5 Hz, P-O-CH_2-$\underline{C}H_3$), 14.92 (s, $\underline{C}H_3$). EI-MS : m/z (%) = 347 (19, $[M+1]^+$), 346 (100, $[M]^+$), 302 (32), 301 (30, $[M-C_2H_5O]^+$), 273 (41, $[M-C_2H_5O-C_2H_4]^+$), 238 (42), 237 (60), 211 (19), 210 (82), 209 (60, $[M-PO-(OC_2H_5)_2]^+$), 184 (12), 183 (12), 169 (23), 145 (14), 142 (11), 115 (11), 105 (50), 103 (17), 102 (30), 89 (27), 82 (12), 81 (32), 80 (54), 77 (26, $[C_6H_5]^+$), 66 (17), 65 (15), 54 (10), 53 (27),

51 (12), 42 (13). HR-MS: m/z Calcd for $C_{16}H_{19}N_4O_3P$: 346.1196. Found: 346.1197. Anal. Calcd for $C_{16}H_{19}N_4O_3P$: C, 55.47; H, 5.53; N, 16.18. Found: C, 55.76; H, 5.61 N, 16.27.

4-(4´-Chlorophenyl)-7-methylpyrazolo[3,2-c][1,2,4]triazin-3-ylphosphonic acid diethyl ester **(11d)**: After refluxing 10.0 mmol of the above described reaction mixture for 15 h column chromatography (ethyl acetate / n-hexane = 10:1) and addition of n-hexane to a solution of **11d** in Et_2O gave pure **11d** as a yellow solid; yield: 880 mg (21 %), mp 117 °C. UV/VIS (CH_2Cl_2): λ (log ε) = 244 (4.58), 284 (3.78), 374 (3.48). IR (KBr): ν [cm^{-1}]= 3445w, 2977m (CH), 1598m, 1554m, 1469s, 1297m, 1244s (P=O), 1217s, 1174m, 1110m, 1048s/1020s (P-O-C), 975s, 948m, 827m, 785m, 723m, 585s, 533m, 497m, 450w. ^{1}H-NMR (299.95 MHz, $CDCl_3$): δ [ppm] = 7.77-7.73 (m, 2H, H-3´, H-5´), 7.61-7.56 (m, 2H, H-2´, H-6´), 7.15 (s, H-8), 4.27-4.11 (m, 4H, P-O-C$\underline{H}_2$-CH_3), 2.57 (s, 3H, CH_3), 1.26 (t, 6H, $^3J_{HH}$ = 7.1 Hz, P-O-CH_2-C$\underline{H}_3$). ^{13}C-NMR (90.56 MHz, $CDCl_3$) : δ [ppm] = 158.52 (s, C-7), 150.99 (d, $^4J_{CP}$ = 2.1 Hz, C-8a), 138.20 (d, $^2J_{CP}$ = 29.9 Hz, C-4), 137.74 (s, C-4´), 134.74 (d, $^1J_{CP}$ = 237.9 Hz, C-3), 131.61 (s, C-2´, C-6´), 128.75 (s, C-3´, C-5´), 125.52 (s, C-1´), 99.51 (s, C-8), 63.66 (d, $^2J_{CP}$ = 6.3 Hz, P-O-$\underline{C}H_2$-CH_3), 16.16 (d, $^3J_{CP}$ = 6.4 Hz, P-O-CH_2-$\underline{C}H_3$), 14.86 (s, $\underline{C}H_3$). ^{31}P-NMR (121.42 MHz, $CDCl_3$): δ [ppm] = 9.51 (s). EI-MS: m/z (%) = 383 (6), 382 (34, $[M+2]^+$, 381 (20, $[M+1]^+$, 380 (100, $[M]^+$, 351 (14), 337 (17), 336 (49, $[M-C_2H_4O]^+$, 335 (28, $[M-C_2H_5O]^+$, 309 (17), 308 (12), 307 (47, $[M-C_2H_4O-C_2H_4]^+$), 292 (11), 274 (15), 273 (32), 272 (45), 271 (64), 246 (27), 245 (25), 244 (75, $[M-PO(OC_2H_5)_2+H]^+$ 243 (31), 237 (52), 217 (12), 209 (39), 203 (21), 176 (10), 162 (13), 154 (11), 139 (15), 138 (18), 137 (20), 136 (31), 123 (18), 114 (19), 111 (13), 82 (16), 81 (47), 80 (66), 66 (36), 65 (21), 54 (14), 53 (38), 42 (15). HR-MS: m/z Calcd for $C_{16}H_{18}N_4O_3ClP$: 380.0806. Found: 380.0807. Anal. Calcd for $C_{16}H_{18}N_4O_3ClP$: C, 50.52; H, 4.77; N, 14.74. Found: 50.52; H, 4.98; N, 14.38.

7-Methylmercapto-4-phenyl[1,2,4]triazolo[3,2-c][1,2,4]triazin-3-ylphosphonic acid diethyl ester **(15a)**: After refluxing 10.0 mmol of the above described reaction mixture for 12 h column chromatography (ethyl acetate / n-hexane = 5:1) gave pure **15a** as a yellow solid; yield: 1.30 g (34 %), mp 164-166 °C. UV/VIS (CH_2Cl_2): λ (log ε) = 230 (4.04), 258 (4.34), 338 (3.91). IR: ν = 3448*s* (O-H), 2980*m*, 1540*m*, 1517*m*, 1481*m*, 1352*s*, 1313*s*, 1275*s* / 1250*s* (P=O), 1113*m*,

1058s / 1025s (P-O-C), 989*m*, 962*m*, 783*m*, 711*m*, 640*m*, 568*m*. ^{1}H-NMR (250.13 MHz, $CDCl_3$): δ = 7.87-7.84 (m, 2H, C-2´, C-6´), 7.70-7.57 (m, 3H, arom. H), 4.28 (m, 4H, P-O-C$\underline{H}_2$-CH_3), 2.73 (s, 3H, S-C$\underline{H}_3$), 1.21 (t, 6H, $^3J_{HH}$ = 7.2 Hz, P-O-CH_2-C$\underline{H}_3$). ^{13}C-NMR (75.43 MHz, $CDCl_3$): δ = 174.00 (s, C-7), 156.28 (d, $^4J_{CP}$ = 2.6 Hz, C-8a), 139.13 (d, $^2J_{CP}$ = 30.4 Hz, C-4), 138.99 (d, $^1J_{CP}$ = 237.0 Hz, C-3), 131.97 (s, arom. C), 129.98 (s, arom. C), 128.29 (s, arom. C), 125.79 (s, C-1´), 63.98 (d, $^2J_{CP}$= 6.5 Hz, P-O-$\underline{C}H_2$-CH_3), 16.07 (d, $^3J_{CP}$ = 6.4 Hz, P-O-CH_2-$\underline{C}H_3$), 14.10 (s, S-$\underline{C}H_3$). ^{31}P-NMR (121.42 MHz, $CDCl_3$): δ = 7.56 (s). EI-MS : m/z (%) = 380 (12, $[M+1]^+$), 379 (74, $[M]^+$), 350 (15), 335 (33), 334 (18, $[M-C_2H_5O]^+$), 332 (13), 306 (31, $[M-C_2H_5O-C_2H_4]^+$), 271 (34), 270 (47), 260 (11), 242 (16), 229 (15), 228 (100), 224 (10), 144 (9), 129 (9), 115 (10), 114 (11), 103 (11), 102 (19), 99 (14), 89 (16), 77 (15), 65 (10), 47 (11). HR-MS: m/z *Calcd* for $C_{15}H_{18}N_5O_3PS$: 379.0867. Found: 379.0867. Anal. Calcd for $C_{15}H_{18}N_5O_3PS$: C, 47.49; H, 4.78; N, 18.46; S, 8.45. Found: C, 47.51; H, 4.73; N, 18.33; S, 8.56.

7-Methylmercapto-4-(4´-methylphenyl)[1,2,4]triazolo[3,2-c][1,2,4]triazin-3-ylphosphonic acid diethyl ester **(15b)**: After refluxing 10.0 mmol of the above described reaction mixture for 15 h column chromatography (ethyl acetate / n- hexane = 2:1) and recrystallisation from Et_2O gave pure **15b** as light yellow needles; yield: 450 mg (11 %), mp 150-151 °C. *UV/VIS* (CH_2Cl_2): λ (log ε) = 254 (4.18), 330 (3.06). *IR* (KBr): ν [cm^{-1}] = *2980m/2903m* (C-H), *1734s*, *1685s*, *1604s*, *1444w*, *1419w*, *1366w*, *1253s* (P=O), *1166m*, *1145m*, *1021s* (P-O-C), *973s*, *835m*, *753m*, *607m*, *518m*, *473m*. ^{1}H-NMR (299.95 MHz, $CDCl_3$): δ [ppm] = 7.78 (d, 2H, $^3J_{HH}$ = 8.1 Hz, H-2´, H-6´), 7.42 (d, 2H, $^3J_{HH}$ = 8.1 Hz, H-3´, H-5´), 4.28-4.11 (m, 4H, P-O-C$\underline{H}_2$-CH_3), 2.74 (s, 3H, S-C$\underline{H}_3$), 2.49 (s, 3H, arom. C$\underline{H}_3$), 1.23 (t, $^3J_{HH}$ = 7.1 Hz, P-O-CH_2-C$\underline{H}_3$). ^{13}C-NMR (62.89 MHz, $CDCl_3$): δ [ppm] = 156.56 (s, C-7), 143.03 (s, C-8a), 139.75 (d, $^2J_{CP}$ = 30.6 Hz, C-4), 139.16 (d, $^1J_{CP}$ = 236.3 Hz, C-3), 137.28 (s, C-4´), 130.30 (s, arom. H), 129.19 (s, arom. CH), 123.01 (s, C-1´), 64.04 (d, $^2J_{CP}$ = 6.2 Hz, P-O-$\underline{C}H_2$-CH_3), 21.79 (s, arom. $\underline{C}H_3$), 16.09 (d, $^3J_{CP}$ = 7.0 Hz, P-O-CH_2-$\underline{C}H_3$), 14.11 (s, S-$\underline{C}H_3$). ^{31}P-NMR (121.42 MHz, $CDCl_3$): δ [ppm] = 7.71 (s). EI-MS : m/z (%) = 395 (4), 394 (13, $[M+1]^+$), 393 (67, $[M]^+$), 364 (12), 349 (14), 346

(15), 334 (40), 320 (21), 306 (12), 285 (16), 284 (35), 270 (33), 243 (14), 242 (100), 210 (6), 183 (7), 158 (10), 143 (10), 116 (19), 115 (14), 103 (14), 99 (14), 91 (19), 81 (14), 65 (11), 47 (8). HR-MS: m/z Calcd for $C_{16}H_{20}N_5O_3PS$: 393.1026. Found: 393.1028. Anal. Calcd for $C_{16}H_{20}N_5O_3PS$: C, 48.84; H, 5.13; N, 17.81; S, 8.13. Found: C, 48.92; H, 5.14; N, 17.74; S, 8.16.

1-[(1H-Indazol-3-yl)hydrazono]-2-(4-chlorophenyl)-2-oxoethylphosphonic acid diethyl ester **(18)**: After refluxing 10.0 mmol of the above described reaction mixture for 12 h column chromatography (ethyl acetate / n-hexane = 2:1) and stirring in n-hexane for 48 h gave pure **18** as an orange solid; yield: 1.07 g (24 %), mp 152-154 °C. UV/VIS (CH_2Cl_2): λ (log ε) = 228 (4.31), 282 (4.24), 368 (4.06). IR: ν = 3289*s* (N-H), 2983*m*, 1636*s* (C=O), 1590*m*, 1559*s*, 1437*m*, 1398*s*, 1294*s*, 1262*s* (P=O), 1173*m*, 1092*m*, 1020*s* (P-O-C), 983*s*, 869*m*, 804*m*, 762*m*, 745*m*, 589*m*. ^{1}H-NMR (250.13 MHz, $CDCl_3$): δ = 13.48 (s, 1H, N-H), 10.52 (s, 1H, N-H), 7.98-6.84 (m, 8H, arom. H), 4.39-4.22 (m, 4H, P-O-C$\underline{H}_2$-CH_3), 1.43-1.23 (m, 6H, P-O-CH_2-C$\underline{H}_3$). ^{13}C-NMR (62.89 MHz, $CDCl_3$): δ = 191.07 (d, $^2J_{CP}$ = 21.7 Hz, C-2), 151.74 (s, C-4´´), 145.26 (s, C-8´), 141.87 (s, C-3´), 137.75 (s, C-1´´), 131.80 (s, C-6´), 131.21 (s, C-2´´, C-6´´), 128.33 (s, C-3´´, C-5´´), 127.99 (d, $^1J_{CP}$ = 155.7 Hz, C-1), 121.87 (s, C-4´), 120.83 (s, C-5´), 113.09 (s, C-9´), 109.94 (s, C-7´), 64.17-63.96 (m, P-O-$\underline{C}H_2$-CH_3), 16.38-16.14 (m, P-O-CH_2-$\underline{C}H_3$). EI-MS : m/z (%) = 436 (12, $[M+2]^+$), 435 (8, $[M+1]^+$), 434 (31, $[M]^+$), 416 (16, $[M-H_2O]^+$), 297 (9, $[M-PO(OC_2H_5)_2]^+$), 295 (31, $[M-^{35}Cl-C_6H_4-CO]^+$), 280 (15), 253 (17), 243 (13), 239 (10), 141 (32, $[^{37}Cl-C_6H_4-CO]^+$), 139 (100, $[^{35}Cl-C_6H_4-CO]^+$), 132 (19), 116 (32), 111 (20, $[^{35}Cl-C_6H_4]^+$), 108 (16), 102 (13), 77 (18). HR-MS: m/z Calcd for $C_{19}H_{20}N_4O_4ClP$: 434.0910. Found: 434.0909. Anal. Calcd for $C_{19}H_{20}N_4O_4ClP$: C, 53.48; H, 4.64; N, 12.89. Found: C, 53.24; H, 4.65; N, 13.05.

3-Diethylphosphonato-4-hydroxy-4-phenylpyrazolo[3,2-c][2H,5H][1,2,4]triazin-8-ylcarbonic acid ethyl ester **(19)**: After refluxing 10.0 mmol of the above described reaction mixture for 6 h column chromatography (ethyl acetate) gave pure **19** as a white, crystalline solid; yield: 450 mg (10 %), mp 192 °C. UV/VIS (CH_2Cl_2): λ (log ε) = 230 (4.08), 306 (4.12). IR: ν = 3303*s*/3144*s* (NH,OH), 2982*m*, 1666*s* (C=O), 1603*s*, 1545*s*, 1287*m*, 1228*s* (P=O), 1162*m*, 1127*m*,

1048*s*/1024*s* (P-O-C), 781*m*, 700*m*, 581*m*, 560*m*. ^{1}H-NMR (299.95 MHz, DMSO-d_6): δ = 8.08 (s, N-H), 7.72 (s, H-7), 7.33 (s, 5H, arom. H), 6.17 (s, O-H), 4.28-4.25 (m, 2H, C-O-C$\underline{H}_2$-CH_3), 3.92-3.78 (m, 4H, P-O-C$\underline{H}_2$-CH_3), 1.29 (m, 3H, C-O-CH_2-C$\underline{H}_3$), 1.09-1.06 (m, 6H, P-O-CH_2-C$\underline{H}_3$). ^{13}C-NMR (62.89 MHz, DMSO-d_6): δ = 161.71 (s, C=O), 140.56 (s, C-8a), 140.16 (s, C-7), 138.52 (s, C-1), 136.99 (d, $^1J_{CP}$ = 266.8 Hz, C-3), 128.02 (s, arom. C), 127.41 (s, arom. C), 126.66 (s, arom. C), 93.63 (s, C-8), 80.79 (d, $^2J_{CP}$ = 26.1 Hz, C-4), 61.82 (d, $^2J_{CP}$ = 5.5 Hz, P-O-$\underline{C}H_2$-CH_3), 59.39 (s, C-O-$\underline{C}H_2$-CH_3), 15.84 (d, $^3J_{CP}$ = 6.9 Hz, P-O-CH_2-$\underline{C}H_3$), 14.22 (s, C-O-CH_2-$\underline{C}H_3$). EI-MS : m/z (%) = 423 (3, $[M+1]^+$), 422 (15, $[M]^+$), 404 (4, $[M-H_2O]^+$), 345 (9, $[M-C_6H_5]^+$), 285 (18, $[M-PO(OC_2H_5)_2]^+$), 271 (9), 239 (4, $[M-PO(OC_2H_5)-C_2H_6O]^+$), 185 (13), 108 (12), 105 (100, $[C_7H_5O]^+$), 77 (19, $[C_6H_5]^+$). HR-MS: m/z Calcd for $C_{18}H_{23}N_4O_6P$: 422.1353. Found: 422.1351. Anal. Calcd for $C_{18}H_{23}N_4O_6P$: C, 51.17; H, 5.49; N, 13.27. Found: C, 51.27, H, 5.65; N, 12.94.

8-Bromo-7-methylpyrazolo[3,2-c][1,2,4]triazin-3-ylphosphonic acid dialkyl esters **(20a,c,d,g)**: General procedure: To a solution of 1.0 mmol of **9c,d**;**11c,d** in dry $CHCl_3$ (60 ml) 1.1 mmol NBS (190 mg) was added under argon. The mixture was refluxed for 1 h and extracted with saturated sodium bicarbonate solution (40 mL). The organic layer was dried ($MgSO_4$), filtered and evaporated.

4-Amino-8-bromo-7-methylpyrazolo[3,2-c][1,2,4]triazin-3-ylphosphonic acid diethyl ester **(20a)**: Column chromatography (ethyl acetate / n-hexane = 5:1) and recrystallisation from Et_2O gave pure **20a** as a yellowish solid; *yield*: 230 mg (63 %), *mp* 149 °C. UV/VIS (CH_2Cl_2): λ (log ε) = 232 (4.41), 304 (3.96), 356 (3.88). IR : ν = 3269*s* (N-H), 2989*m*, 1625*s*, 1560*s*, 1465*m*, 1390*m*, 1218*s* (P=O), 1171*m*, 1080*m*, 1026*s* (P-O-C), 978*m*, 861*m*, 797*m*, 761*s*, 621*m*, 568*s*, 497*s*. ^{1}H-NMR (250.13 MHz, $CDCl_3$): δ = 8.59 (1H, N-H), 6.98 (1H, N-H), 4.40-4.18 (m, 4H, P-O-C$\underline{H}_2$-CH_3), 2.52 (s, 3H, C$\underline{H}_3$), 1.37 (t, 6H, $^3J_{HH}$ = 6.9 Hz, P-O-CH_2-C$\underline{H}_3$). ^{13}C-NMR (62.89 MHz, $CDCl_3$): δ = 155.41 (s, C-7), 145.88 (s, C-8a), 142.63 (d, $^2J_{CP}$ = 31.7 Hz, C-4), 117.18 (d, $^1J_{CP}$ = 236.6 Hz, C-3), 86.66 (s, C-8), 64.15 (d, $^2J_{CP}$ = 6.1 Hz, P-O-$\underline{C}H_2$-H_3), 16.21 (d, $^3J_{CP}$ = 6.2 Hz, P-O-CH_2-$\underline{C}H_3$), 13.12 (s, $\underline{C}H_3$ at C-7). EI-MS : m/z (%) = 366 (8), 365 (66, [^{81}Br-

M]$^+$), 364 (11), 363 (67, [^{79}Br-M]$^+$), 321 (40 [^{81}Br-M-C_2H_4O]$^+$), 319 (44, [^{79}Br-M-C_2H_4O]$^+$), 293 (10), 292 (71, [^{81}Br-M-C_2H_4O-C_2H_5]$^+$), 291 (18), 290 (69), [^{79} Br-M-C_2H_4O-C_2H_5]$^+$), 289 (10), 257 (80), 256 (42), 255 (82), 254 (32), 230 (10), 229 (100, [^{81}Br-M-PO(OC_2H_5)$_2$+H]$^+$), 228 (16) ,227 (96, [^{79}Br-M-PO(OC_2H_5)$_2$+H]$^+$), 202 (14), 200 (11), 177 (57), 176 (14), 175 (62), 146 (13), 144 (11), 121 (12), 109 (11), 108 (42), 104 (10), 95 (15), 93 (20), 82 (39), 81(44), 66 (39), 65 (39), 64 (21), 55(11), 54 (15), 53 (17), 43 (12), 42 (38), 41 (27). HR-MS: m/z Calcd for $C_{10}H_{15}N_5O_3{}^{79}BrP$: 363.0096. Found: 363.0096. Anal. Calcd for $C_{10}H_{15}N_5O_3{}^{79}BrP$: C, 32.98, H, 4.15; N, 19.23. Found: C, 33.08; H, 4.22; N, 19.07.

8-Bromo-7-methyl-4-phenylpyrazolo[3,2-c][1,2,4]triazin-3-ylphosphonic acid diethyl ester (**20c**): Column chromatography (ethyl acetate / n-hexane = 5:1) gave pure **20c** as a yellow solid; yield: 1.00 g (78 %), mp 103 °C. UV/VIS (CH_2Cl_2): λ (log ε) = 230*sh* (4.08), 252 (4.52), 286 (3.69), 392 (3.44). IR (KBr): ν [cm^{-1}] = 3448*m*, 3162*m*, 3058*m*, 2926*s*, 2855*m*, 1772*m*, 1700*s*, 1511*m*, 1465*m*, 1375*m*, 1288*m*, 1251*s* (P=O), 1229*m*, 1178*s*, 1121*w*, 1050*s*, 1022*s* (P-O-C), 962*m*, 822*m*, 796*m*, 777*m*, 694*m*, 651*m*, 588*m*, 540*m*. ^{1}H-NMR (250.13 MHz, $CDCl_3$): δ [ppm]= 7.78-7.74 (m, arom. H), 7.64-7.58 (m, 3H, arom. H), 4.24-4.07 (m, 4H, P-O-C$\underline{H}_2$-CH_3), 2.54 (s, 3H, C$\underline{H}_3$ at C-7), 1.21 (t, 6H, $^3J_{HH}$ = 7.1 Hz, P-O-CH_2-C$\underline{H}_3$). ^{13}C-NMR (90.56 MHz, $CDCl_3$): δ [ppm]= 156.96, C-7), 147.31 (d, $^4J_{CP}$ = 2.2 Hz, C-8a), 139.44 (d, $^2J_{CP}$ = 29.3 Hz, C-4), 135.94 (d, $^1J_{CP}$ = 238.9 Hz, C-3), 131.63 (s, arom. CH), 130.08 (s, arom. CH), 128.46 (s, arom. CH), 126.27 (s, C-1´), 89.06 (s, C-8), 63.84 (d, $^2J_{CP}$ = 6.5 Hz, P-O-$\underline{C}H_2$-CH_3), 16,09 (d, $^3J_{CP}$ = 7.2 Hz, P-O-CH_2-$\underline{C}H_3$), 13.41 (s, $\underline{C}H_3$ at C7). EI-MS : m/z (%) = 427 (16), 426 (82, [^{81}Br-M]$^+$), 25 (15), 424 (100, [^{79}Br-M]$^+$), 382 (35, [^{81}Br-M-C_2H_4O]$^+$), 381 (25), 380 (35, [^{79}Br-M-C_2H_4O]$^+$), 379 (19), 353 (33, [^{81}Br-M-C_2H_4O-C_2H_5]$^+$), 351 (38, [^{79}Br-M-C_2H_4O-C_2H_5]$^+$), 318 (32), 317 (59), 316 (36), 315 (52), 289 (37, [^{81}Br-M-PO(OC_2H_5)$_2$]$^+$), 287 (31, [^{79}Br-M-PO(OC_2H_5)$_2$]$^+$), 273 (15), 249 (16), 237 (16), 210 (11), 209 (41), 182 (35), 160 (35), 158 (33), 144 (11), 115 (10),104 (10), 103 (13), 102 (42), 89 (18), 81(18, [^{81}Br]$^+$), 79 (11, [^{79}Br]$^+$), 65 (12). HR-MS: m/z Calcd for $C_{16}H_{18}N_4O_3{}^{79}BrP$: 424.0299. Found: 424.0298. Anal. Calcd for $C_{16}H_{18}N_4O_3{}^{79}BrP$: C, 45.19; H, 4.27; N, 13.18. Found: C, 45.06, H, 4.27; N, 13.13.

8-Bromo-4-(4′-chlorophenyl)-7-methylpyrazolo[3,2-c][1,2,4]triazin-3-ylphosphonic acid diethyl ester **(20d)**: Column chromatography (ethyl acetate / n-hexane = 10:1) and stirring in Et_2O for 12 h gave pure **20d** as yellow needles; yield: 135 mg (93 %), mp 120 °C. UV/VIS (CH_2Cl_2): λ (log ε) = 228sh (4.07), 252 (4.51), 294 (3.79), 392 (3.45). IR (KBr): ν [cm^{-1}] = 3448*m*, 3088*w*, 2985*m* (arom. H), 1596*m*, 1533*m*, 1513*m*, 1480*s*, 1404*w*, 1388*w*, 1286*m*, 1255*s* (P=O), 1221*m*, 1171*m*, 1159*w*, 1095*m*, 1053*s*, 1009*s* (P-O-C), 978*s*, 837*m*, 801*m*, 773*m*, 588*s*, 547*s*, 509*m*. ^{1}H-NMR (250.13 MHz, $CDCl_3$): δ [ppm]= 7.73 (d, 2H, $^3J_{HH}$ = 8.5 Hz, H-3′, H-5′), 7.58 (d, 2H, $^3J_{HH}$ = 8.5 Hz, H-2′, H-6′), 4.28-4.12 (m, 4H, P-O-C$\underline{H}_2$-CH_3), 2.55 (s, 3H, C$\underline{H}_3$), 1.25 (t, 6H, $^3J_{HH}$ = 7.0 Hz, P-O-CH_2-C$\underline{H}_3$). ^{13}C-NMR (90.56 MHz, $CDCl_3$): δ [ppm]= 157.08 (s, C-7), 147.32 (s, C-8a), 138.39 (d, $^2J_{CP}$ = 29.2 Hz, C-4). 138.16 (s, C-4′), 135.91 (d, $^1J_{CP}$ = 237.0 Hz, C-3), 131.66 (s, C-2′, C-6′), 128.89 (s, C-3′, C-5′), 124.60 (s, C-1′), 89.37 (s, C-8), 63.92 (d, $^2J_{CP}$ = 6.9 Hz, P-O-$\underline{C}H_2$-CH_3), 16.16 (d, $^3J_{CP}$ = 6.4 Hz, P-O-CH_2-$\underline{C}H_3$), 13.37 (s, $\underline{C}H_3$ at C-7). EI-MS : m/z (%) = 463 (5), 462 (24, [^{81}Br-^{37}Cl-M]$^+$), 461 (17), 460 (100, [^{81}Br-^{35}Cl-M/^{79}Br-^{37}Cl-M]$^+$), 459 (18), 458 (76, [^{79}Br-^{35}Cl-M]$^+$), 432 (13), 418 (11), 417 (13), 416 (55, [^{81}Br-^{35}Cl-M-C_2H_4O/^{79}Br-^{37}Cl-M-C_2H_4O]$^+$), 415 (27), 414 (37), 387 (38), 385 (33), 380 (35), 351 (72), 349 (50), 317 (44), 315 (40), 289 (39), 287 (41), 271 (38), 244 (36), 242 (38), 216 (34), 160 (44), 158 (47), 139 (34), 138 (34), 137 (34), 136 (77), 123 (31), 114 (27), 111 (22), 81 (65), 65 (42), 53 (25), 42 (23). HR-MS: m/z Calcd for $C_{16}H_{17}N_4O_3{}^{79}Br^{35}ClP$: 457.9910. Found: 457.9910. Anal. Calcd for $C_{16}H_{17}N_4O_3{}^{79}Br^{35}ClP$: C, 41.81; H, 3.73; N, 12.19. Found: C, 42.06; H, 3.88; N, 11.94.

4-Amino-8-bromo-7-methylpyrazolo[3,2-c][1,2,4]triazin-3-ylphosphonic acid diisopropyl ester **(20g)**: Column chromatography (ethyl acetate / n-hexane = 5:1) and recrystallisation from Et_2O gave pure **20g** as a yellow solid; yield: 190 mg (48 %), mp 145 °C. UV/VIS (CH_2Cl_2): λ (log ε) = 234 (4.31), 306 (3.89), 356 (3.81). IR (KBr): ν [cm^{-1}] = 3271*s*/3141*s* (N-H), 2984*s*, 1629*s*, 1565*s*, 1463*s*, 1388*s*, 1341*m*, 1216*s* (P=O), 1172*s*, 1142*m*, 1101*s*, 1004*s* (P-O-C), 887*m*, 860*m*, 780*m*, 756*m*, 702*m*, 621*m*, 571*s*, 511*m*, 440*m*. ^{1}H-NMR (250.13 MHz, $CDCl_3$): δ [ppm]= 8.65 (1H, N-H), 6.62 (1H, N-H), 4.85-4.74 (m, 2H, P-O-C$\underline{H}_2$-CH_3), 2.52 (s, 3H, C$\underline{H}_3$ at C-7), 1.36 (d, 6H, $^3J_{HH}$ = 6.1 Hz, P-O-CH-($C\underline{H}_3$)$_2$), 1.29 (d, 6H, $^3J_{HH}$ = 6.1 Hz, P-O-CH-

($C\underline{H}_3)_2$). ^{13}C-NMR (90.56 MHz, $CDCl_3$): δ [ppm]= 155.33 (s, C-7), 145.83 (s, C-8a), 142.31 (d, $^2J_{CP}$ = 31.6 Hz, C-4), 118.20 (d, $^1J_{CP}$ = 235.5 Hz, C-3), 86.70 (s, C-8), 73.17 (d, $^2J_{CP}$ = 6.3 Hz, P-O-$\underline{C}$H-$(H_3)_2$), 23.97-23.74 (m, P-O-CH-$(\underline{C}H_3)_2$), 13.13 (s, $\underline{C}H_3$ at C-7). EI-MS : m/z (%) = 393 (24, $[^{81}Br\text{-}M]^+$), 391 (24, $[^{79}Br\text{-}M]^+$), 335 (22, $[^{81}Br\text{-}M\text{-}C_3H_6O]^+$), 333 (22, $[^{79}Br\text{-}M\text{-}C_3H_6O]^+$), 309 (100, $[^{81}Br\text{-}M\text{-}2C_3H_6]^+$), 307 (94, $[^{79}Br\text{-}M\text{-}2C_3H_6O]^+$), 293 (18, $[^{81}Br\text{-}M\text{-}C_3H_6\text{-}C_3H_6O]^+$), 292 (22), 291 (32, $[^{79}Br\text{-}M\text{-}C_3H_6\text{-}C_3H_6O]^+$), 290 (22), 289 (17), 229 (19, $[^{81}Br\text{-}M\text{-}PO(O\text{-}i\text{-}C_3H_7)_2{+}H]^+$), 227 (20, $[^{79}Br\text{-}M\text{-}PO(O\text{-}i\text{-}C_3H_7)_2{+}H]^+$), 177 (17), 175 (20), 146(8), 121 (9), 108 (20), 82 (35), 66 (27), 65 (14), 43 (82), 42 (27), 41 (35). HR-MS: m/z Calcd for $C_{12}H_{19}N_5O_3{}^{79}BrP$: 391.0407. Found: 391.0405. Anal. Calcd for $C_{12}H_{19}N_5O_3{}^{79}BrP$: C, 36.75; H, 4.88; N, 17.86. Found: C, 37.05; H, 5.07; N, 17.78.

8-Iodo-7-methylpyrazolo[3,2-c][1,2,4]triazin-3-ylphosphonic acid dialkyl esters **(20b,e,f,h)**: General procedure: To a solution of 1.0 mmol of **9c,d**;**11c,e** in dry $CHCl_3$ (40 mL) 5.0 mmol (1.12 g) of *N*-iodosuccinimide were added under argon. The mixture was refluxed for 4 to 7 h and then washed with saturated sodium sulfite solution (40 mL), saturated sodium bicarbonate solution (40 mL) and water (40 mL). The organic layer was dried ($MgSO_4$), filtered and evaporated.

4-Amino-8-iodo-7-methylpyrazolo[3,2-c][1,2,4]triazin-3-ylphosphonic acid diethyl ester **(20b)**: The solution of **9c** (1.0 mmol) in $CHCl_3$ (30 mL) was refluxed for 2.5 h and worked up according to the general procedure. Column chromatography (ethyl acetate / n-hexane = 5:1) and stirring in Et_2O for 24 h gave pure **20b** as a light brown solid; yield: 180 mg (43%), mp 142 °C. UV/VIS (CH_2Cl_2): λ (log ε)= 238 (4.29), 308 (3.93), 358 (3.88). IR: ν = 3376*m*/3270*s* (N-H), 2977*m*, 1606*s*, 1534*s*, 1384*m*, 1220*s* (P=O),1167*m*, 1078*m*, 1023*s* (P-O-C), 983*m*, 776*m*, 565*m*, 494*m*. ^{1}H-NMR (250.13 MHz, $CDCl_3$): δ = 8.55 (1H, N-H), 6.50 (1H, N-H), 4.33-4.17 (m, 4H, P-O-$C\underline{H}_2$-CH_3), 2.55 (s, 3H, $C\underline{H}_3$ at C-7), 1.39-1.33 (m, 6H, P-O-CH_2-$C\underline{H}_3$). ^{13}C-NMR (62.89 MHz, DMSO-d_6): δ = 157.22 (s, C-7), 148.32 (s, C-8a), 142.87 (d, $^2J_{CP}$ = 32.8 Hz, C-4), 116.86 (d, $^1J_{CP}$ = 235.3 Hz, C-3), 63.00 (d, $^2J_{CP}$ = 5.9 Hz, P-O-$\underline{C}H_2$-CH_3), 54.88 (s, C-8), 15.96 (d, $^3J_{CP}$ = 5.8 Hz, P-O-CH_2-$\underline{C}H_3$), 14.45 (s, $\underline{C}H_3$ at C-7). EI-MS : m/z (%) = 412 (15, $[M+1]^+$), 411 (100, $[M]^+$), 367 (40, $[M\text{-}C_2H_4O]^+$), 338 (50), 303 (73), 302 (34), 275 (91, [M-

$PO(OC_2H_5)_2+H]^+$), 223 (47), 108 (17), 82 (17), 81 (15), 66 (17), 65 (22), 64 (14), 54 (9), 41 (9), 40 (10). HR-MS: m/z Calcd for $C_{10}H_{15}N_5O_3IP$: 410.9956. Found: 410.9957. Anal. Calcd for $C_{10}H_{15}N_5O_3IP$: C, 29.21; H, 3.68; N, 17.03. Found: C, 29.56; H, 3.56; N, 16.83.

8-Iodo-7-methyl-4-phenylpyrazolo[3,2-c][1,2,4]triazin-3-ylphosphonic acid diethyl ester **(20e)**: Refluxing time: 4 h. Column chromatography (ethyl acetate), stirring in Et_2O for 24 h and recrystallisation from the same solvent gave pure **20e** as a yellow solid; yield: 160 mg (34 %), mp 132 °C. UV/VIS (CH_2Cl_2): λ (log ε) = 244 (4.71), 282 (3.78), 374 (3.56). IR (KBr): ν [cm^{-1}] = 3447*m*, 2986*m*, 1558*m*, 1472*m*, 1286*m*, 1245*m*, 1217*m*, 1057*s*, 1025*s*, 982*m*, 952*m*, 776*m*, 750*m*, 693*m*, 585*m*. ^{1}H-NMR (250.13 MHz, $CDCl_3$): δ [ppm]= 7.78-7.74 (m, 2H, arom. H), 7.62-7.59 (m, 3H, arom. H), 4.25-4.07 (m, 4H, P-O-C$\underline{H}_2$-CH_3), 2.55 (s, 3H, C$\underline{H}_3$ at C-7), 1.21 (t, 6H, $^3J_{HH}$ = 7.1 Hz, P-O-CH_2-C$\underline{H}_3$). ^{13}C-NMR (62.89 MHz, $CDCl_3$): δ [ppm]= 160.30 (s, C-7), 149.85 (s, C-8a), 139.52 (d, $^2J_{CP}$ = 29.4 Hz, C-4), 136.31 (d, $^1J_{CP}$ = 238.1 Hz, C-3), 131.60 (s, arom. CH), 130.12 (s, arom. CH), 128.44 (s, arom. CH), 126.40 (s, C-1´), 63.78 (d, $^2J_{CP}$ = 6.4 Hz, P-O-$\underline{C}H_2$-CH_3), 56.79 (s, C-8), 16.11 (d, $^3J_{CP}$ = 7.2 Hz, P-O-CH_2-$\underline{C}H_3$), 15.19 (s, $\underline{C}H_3$ at C-7). EI-MS : m/z (%) = 473 (19, $[M+1]^+$), 472 (100, $[M]^+$), 428 (40, $[M-C_2H_4O]^+$), 427 (21), 399 (39), 364 (47), 363 (61), 336 (16), 335 (35, $[M-PO(OC_2H_5)_2]^+$), 273 (11), 237 (15), 210 (12), 209 (41), 208 (18), 206 (26), 183 (10), 182 (39), 165 (22), 157 (11), 144 (16), 115 (22), 105 (11), 103 (14), 102 (40), 89 (37), 81 (30), 79 (55), 77 (17), 66 (11), 65 (23), 51 (8), 42 (8). HR-MS: m/z Calcd for $C_{16}H_{18}N_4O_3IP$: 472.0160. Found: 472.0161. Anal. Calcd for $C_{16}H_{18}N_4O_3IP$: C, 40.70; H, 3.84; N, 11.86. Found: C, 40.98; H, 4.02; N, 11.52.

8-Iodo-7-methyl-4-(4´-nitrophenyl)pyrazolo[3,2-c][1,2,4]triazin-3-ylphosphonic acid diethyl ester **(20f)**: Refluxing time: 7 h. Column chromatography (ethyl acetate / n-hexane = 5:1) and recrystallisation from Et_2O gave pure **20f** as an orange solid; yield: 80 mg (30 %), mp 151 °C. UV/VIS (CH_2Cl_2): λ (log ε) = 230 (4.16), 256 (4.51), 302*sh* (3.86), 396 (3.54). IR (KBr): ν [cm^{-1}] = 3123*m*/3101*m*/2901*m* (arom. H), 1603*m*, 1555*s*, 1521*s*, 1472*s*, 1443*m*, 1394*m*, 1348*s*, 1308*m*, 1247*s*/1221*s* (P=O), 1161*m*, 1104*m*, 1057*s*/1026*s* (P-O-C), 977*s*, 948*s*, 917*m*, 849*s*, 811*m*, 772*m*, 752*m*, 693*m*, 586*s*, 534*m*, 466*m*. ^{1}H-NMR (250.13 MHz, $CDCl_3$): δ [ppm]= 8.47-

8.43 (m, 2H, H-3′, H-5′), 7.95-7.90 (m, 2H, H-2′, H-6′), 4.30-4.14 (m, 4H, P-O-C$\underline{H}_2$-CH$_3$), 2.56 (s, 3H, C$\underline{H}_3$ at C-7), 1.27 (t, 6H, $^3J_{HH}$ = 6.9 Hz, P-O-CH$_2$-C$\underline{H}_3$). ^{13}C-NMR (62.89 MHz, $CDCl_3$): δ [ppm]= 160.83 (s, C-7), 155.74 (s, C-8a), 149.72 (d, $^2J_{CP}$ = 18.3 Hz, C-4), 137.72 (s, C-4′), 135.37 (d, $^1J_{CP}$ = 221.4 Hz, C-3), 132.61 (s, C-1′), 131.52 (s, C-2′, C-6′), 123.55 (s, C-3′, C-5′), 64.08 (d, $^2J_{CP}$ = 6.8 Hz, P-O-$\underline{C}H_2$-CH$_3$), 57.77 (s, C-8), 16.20 (d, $^3J_{CP}$ = 6.6 Hz, P-O-CH$_2$-$\underline{C}H_3$), 15.14 (s, $\underline{C}H_3$ at C-7). EI-MS : m/z (%) = 518 (19, $[M+1]^+$), 517 (100, $[M]^+$), 473 (35, $[M-C_2H_4O]^+$), 462 (20), 444 (31), 433 (16), 408 (30), 398 (25), 397 (26), 392 (30), 381 (28), 363 (25), 335 (31), 334 (32), 254 (15), 216 (14), 208 (18), 206 (35), 191 (11), 165 (20), 139 (17), 114 (24), 81 (45), 79 (98), 65 (32), 51 (9), 42 (12). HR-MS: m/z Calcd for $C_{16}H_{17}N_5O_5IP$: 517.0010. Found: 517.0010. Anal. Calcd for $C_{16}H_{17}N_5O_5IP$: C, 37.16; H, 3.31; N, 13.54. Found: C, 37.04; H, 3.31; N, 13.75.

4-Amino-8-iodo-7-methylpyrazolo[3,2-c][1,2,4]triazin-3-ylphosphonic acid diisopropyl ester **(20h)**: Refluxing time: 4 h. Column chromatography (ethyl acetate / n-hexane = 5:1) and stirring in Et_2O for 2 h gave pure **20h** as a brown solid; yield: 655 mg (74 %), mp 125-127 °C. UV/VIS (CH_2Cl_2): λ (log ε) = 238 (4.24), 306 (3.87), 358 (3.84). IR (KBr): ν [cm^{-1}] = 3268*s*/3137*s* (N-H), 2980*m*, 1700*m*, 1627*s*, 1559*s*, 1451*m*, 1386*m*, 1339*m*, 1217*s* (P=O), 1166*m*, 1100*m*, 1002*s* (P-O-C), 887*w*, 851*m*, 779*m*, 756*m*, 701*w*, 620*w*, 566*m*, 509*m*, 429*w*. ^{1}H-NMR (250.13 MHz, $CDCl_3$): δ [ppm]= 8.61 (1H, N-H), 6.51 (1H, N-H), 4.83-4.70 (m, 2H, P-O-C$\underline{H}$-(CH$_3$)$_2$), 2.52 (s, 3H, C$\underline{H}_3$ at C-7), 1.34 (d, 6H, $^3J_{HH}$ = 6.1 Hz, P-O-CH-(C$\underline{H}_3$)$_2$), 1.29 (d, 6H, $^3J_{HH}$ = 6.1 Hz, P-O-CH-(C$\underline{H}_3$)$_2$). ^{13}C-NMR (62.89 MHz, $CDCl_3$): δ [ppm]= 158.51 (s, C-7), 148.41 (s, C-8a), 142.38 (d, $^2J_{CP}$ = 30.8 Hz, C-4), 118.47 (d, $^1J_{CP}$ = 236.4 z, C-3), 73.22 (d, $^2J_{CP}$ = 6.2 Hz, P-O-$\underline{C}$H-(CH$_3$)$_2$), 23.99-23.75 (m, P-O-CH-($\underline{C}$H$_3$)$_2$), 14.85 (s, $\underline{C}H_3$ at C-7). EI-MS : m/z (%) = 440 (7, $[M+1]^+$), 439 (45, $[M+1]^+$), 381 (27), 356 (10), 355 (100, $[M-2\ C_3H_6]^+$), 339 (17, $[M-C_3H_6O-C_3H_6]^+$), 338 (24), 337 (18), 275 (22, $[M-PO(O\text{-}i\text{-}C_3H_7)_2+H]^+$), 223 (12), 82 (10), 66 (12), 65 (11), 43 (33), 41 (16). HR-MS: m/z Calcd for $C_{12}H_{19}N_5O_3IP$: 439.0269. Found: 439.270. Anal. calcd for $C_{12}H_{19}N_5O_3IP$: C, 32.82; H, 4.36; N, 15.95. Found: C, 33.03; H, 4.55; N, 15.95.

4-Amino-7-methyl-8-phenylethinylpyrazolo[3,2-c][1,2,4]triazin-3-ylphosphonic acid diethyl ester **(21a)**: To a solution of **20b** (1.0 mmol, 411 mg) in freshly distilled $(i\text{-Pr})_2NH$ (40 mL) bis(triphenylphosphine)palladium-II chloride (0.4 mmol, 280 mg) and triphenylphosphine (0.8 mmol, 210 mg) were added. After 30 min at rt copper-I iodide (0.4 mmol, 80 mg) was added to the mixture. After 30 min phenylacetylene (1.5 mmol, 152 mg) was added, the mixture was refluxed for 4.5 h and then evaporated. The pure product was isolated after column chromatography (ethyl acetate / n-hexane = 1:1), stirring in Et_2O for 3 h and in n-hexane for 24 h as a yellow solid.yield: 80 mg (20%), mp 75 °C. UV/VIS (CH_2Cl_2): λ (log ε) = 230 (4.32), 264*sh* (4.03), 328*sh* (3.39). IR: ν = 3051*m*, 1479*m*, 1433*s*, 1261*m*, 1093*m*, 1027*m*, 823*m*, 741*s*, 693*s*, 517*s*. ^{1}H-NMR (250.13 MHz, $CDCl_3$): δ = 9.94 (s,1H, N-H), 8.53 (s,1H, N-H), 7.81-7.31 (m, 5H, arom. H), 4.40-4.21 (m, 4H, P-O-C$\underline{H}_2$-CH_3), 2.61 (s, 3H, C$\underline{H}_3$ at C-7), 1.36 (t, 6H, $^3J_{HH}$ = 7.1 Hz, P-O-CH_2-C$\underline{H}_3$). ^{13}C-NMR (90.56 MHz, $CDCl_3$): δ = 158.38 (s, C-7), 148.15 (s, C-8a), 142.50 (d, $^2J_{CP}$ = 31.4 Hz, C-4), 133.90 (s, C-4´), 130.79 (s, arom. C), 129.94 (s, arom. C), 122.84 (s, C-1´), 117.44 (d, $^1J_{CP}$ = 236.7 Hz, C-3), 95.86 (s, sp-C), 94.92 (s, sp-C), 77.97 (s, C-7), 63.84 (d, $^2J_{CP}$ = 5.8 Hz, P-O-$\underline{C}H_2$-CH_3), 15.90 (d, $^3J_{CP}$ = 6.6 Hz, P-O-CH_2-$\underline{C}H_3$), 13.13 (s, $\underline{C}H_3$ at C-7). EI-MS : m/z (%) = 386 (21, $[M+1]^+$), 385 (100, $[M]^+$), 311 (9), 277 (16), 249 (43), 197 (20), 140 (10), 139 (26), 108 (6), 82 (7). HR-MS: m/z Calcd for $C_{18}H_{20}N_5O_3P$: 385.1302. Found: 385.1300. Anal. Calcd for $C_{18}H_{20}N_5O_3P$: C, 56.10; H, 5.23; N, 18.17. Found: C, 56.33; H, 5.16; N, 18.30.

7-Methyl-4-phenyl-8-phenylethinylpyrazolo[3,2-c][1,2,4]triazin-3-ylphosphonic acid diethyl ester **(21b)**: To a solution of **20e** (1.0 mmol, 411 mg) in freshly distilled $(i\text{-Pr})_2NH$ (40 mL) bis(triphenylphosphine)palladium-II chloride (0.4 mmol, 280 mg) and triphenylphosphine (0.8 mmol, 210 mg) were added. After 30 min at rt copper-I iodide (0.4 mmol, 80 mg) was added to the mixture followed after 30 min by phenylacetylene (1.5 mmol, 152 mg). The mixture was heated to 70 °C for 4 h and then evaporated. The pure product was isolated after column chromatography (ethyl acetate / n-hexane =5:1) and stirring in Et_2O for 3 h and in n-hexane for 24 h as a light brown solid; yield: 50 mg (11 %), mp 89-90 °C. UV/VIS (CH_2Cl_2): λ (log ε) = 230 (4.30), 252*sh* (4.37), 262 (4.36), 288 (4.40), 330 (4.02), 420 (3.62). IR (KBr): ν [cm^{-1}] = 3446*m*, 3163*m*, 3061*m*, 2987*m*, 1773*m*, 1700*m*, 1635*m*, 1500*m*, 1479*m*, 1259*s* (P=O), 1184*m*,

1053*s*/1028*s* (P-O-C), 768*m*, 698*m*, 525*m*. ^{1}H-NMR (250.13 MHz, $CDCl_3$): δ [ppm]= 7.81-7.36 (m, 10 H, arom. H), 4.26-4.07 (m, 4H, P-O-C$\underline{H}_2$-CH_3), 2.65 (s, 3H, C$\underline{H}_3$ at C-7), 1.24-1.18 (m, 6H, P-O-CH_2-C$\underline{H}_3$). ^{13}C-NMR (62.89 MHz, $CDCl_3$): δ [ppm]= 160.21 (s, C-7), 149.78 (s, C-8a), 139.57 (d, $^{2}J_{CP}$ = 29.1 Hz, C-4), 138.36 (s, C-1′), 134.58 (s, C-1′′), 131.73 (s, arom. C), 131.59 (s, arom. C), 130.13 (s, arom. C), 128.62 (s, arom. C), 128.42 (s, arom. C), 124.89 (d, $^{1}J_{CP}$ = 235.8 Hz, C-3), 97.27 (s, sp-C), 97.11 (s, sp-C), 71.74 (s, C-8), 63.76 (d, $^{2}J_{CP}$ = 6.2 Hz, P-O-$\underline{C}H_2$-CH_3), 16.11 (d, $^{3}J_{CP}$ = 6.7 Hz, P-O-CH_2-$\underline{C}H_3$), 13.73 (s, $\underline{C}H_3$ at C-7). EI-MS: m/z (%) = 447 (25, $[M+1]^+$), 446 (89, $[M]^+$), 373 (11, $[M-C_2H_5O-C_2H_4]^+$), 338 (14), 337 (24), 310 (35), 309 (56, $[M-PO(OC_2H_5)_2]^+$), 165 (10), 140 (23), 139 (100), 102 (17), 81 (13), 77 (11). HR-MS: m/z Calcd for $C_{24}H_{23}N_4O_3P$: 446.1508. Found: 446.1508. Anal. Calcd for $C_{24}H_{23}N_4O_3P$: C, 64.57; H, 5.19; N, 12.55. Found: C, 64.55; H, 5.23; N, 12.71.

4-Amino-7-methyl-8-phenylethinylpyrazolo[3,2-c][1,2,4]triazin-3-ylphosphonic acid diisopropyl ester **(21c)**: To a solution of **20h** (0.5 mmol, 220 mg) in freshly distilled (*i*-Pr)$_2$NH (30 mL) bis(triphenylphosphine)palladium-II chloride (0.05 mmol, 35 mg) and triphenylphosphine (0.1 mmol, 26 mg) were added. After 30 min at rt this was followed by copper-I iodide (0.05 mmol, 10 mg). After 30 min phenylacetylene (0.75 mmol, 76 mg) was added, the mixture was refluxed for 5 h and then evaporated. The pure product was isolated after column chromatography (acetic acid ethyl ester / n-hexane = 4:1), stirring in Et_2O for 3 h and in n-hexane for 24 h as a yellow solid; yield: 80 mg (38 %), mp 207 °C. UV/VIS (CH_2Cl_2): λ (log ε) = 232 (4.42), 280 (4.14), 308 (4.08), 380 (4.02). IR (KBr): ν [cm^{-1}] = 3271*s*/3139*s* (N-H), 2983*m*, 1628*s*, 1560*s*, 1463*m*, 1387*m*, 1343*m*, 1217*s* (P=O), 1172*m*, 1101*m*, 1004*s* (P-O-C), 860*m*, 780*m*, 743*m*, 701*w*, 621*w*, 571*m*, 511*m*. ^{1}H-NMR (250.13 MHz, $CDCl_3$): δ [ppm]= 8.68 (1H, N-H), 7.60-7.31 (m, 5H, arom. H), 6.91 (1H, N-H), 4.86-4.77 (m, 2H, P-O-C$\underline{H}$-$(CH_3)_2$), 2.62 (s, 3H, C$\underline{H}_3$ at C-7), 1.38 (d, 6H, $^{3}J_{HH}$ = 6.1 Hz, P-O-CH-(C$\underline{H}_3)_2$), 1.32 (d, 6H, $^{3}J_{HH}$ = 6.1 Hz, P-O-CH-(C$\underline{H}_3)_2$). ^{13}C-NMR (62.89 MHz, $CDCl_3$): δ [ppm]= 158.78 (s, C-7), 148.47 (s, C-8a), 142.47 (d, $^{2}J_{CP}$ = 30.9 Hz, C-4), 131.60 (s, arom. C), 129.67 (s, arom. C), 128.33 (s, arom. C), 123.32 (s, C-1), 118.93 (d, $^{1}J_{CP}$ = 235.0 Hz, C-3), 96.20 (s, sp-C), 95.33 (s, sp-C), 78.27 (s, C-8), 73.20 (d, $^{2}J_{CP}$ = 6.2 Hz, P-O-$\underline{C}$H-$(CH_3)_2$), 24.00-23.73 (m, P-O-CH-($\underline{C}H_3)_2$), 13.44 (s, $\underline{C}H_3$ at

C-7). EI-MS : m/z (%) = 414 (18, $[M+1]^+$), 413 (76, $[M]^+$), 371 (13, $[M-C_3H_6]^+$), 330 (16), 329 (100, $[M-2\ C_3H_6]^+$), 312 (17, $[M-C_8H_5]^+$), 311 (22), 249 (16, $[M-PO(O-i-C_3H_7)_2+H]^+$), 197 (10), 165 (10), 139 (22), 43 (9). HR-MS: m/z Calcd for $C_{20}H_{24}N_5O_3P$: 413.1617. Found: 413.1617. Anal. Calcd for $C_{20}H_{24}N_5O_3P$: C, 58.11; H, 5.85; N, 16.94. Found: C, 58.21; H, 5.81; N, 16.84.

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