

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-ylphosphonic acid dialkyl esters (**5-7**), pyrazolo[3,2-*c*][1,2,4]triazin-3-ylphosphonic 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 described. 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

Previously¹ 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*]indazoles², 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 Novinson³ or Ege⁴ 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

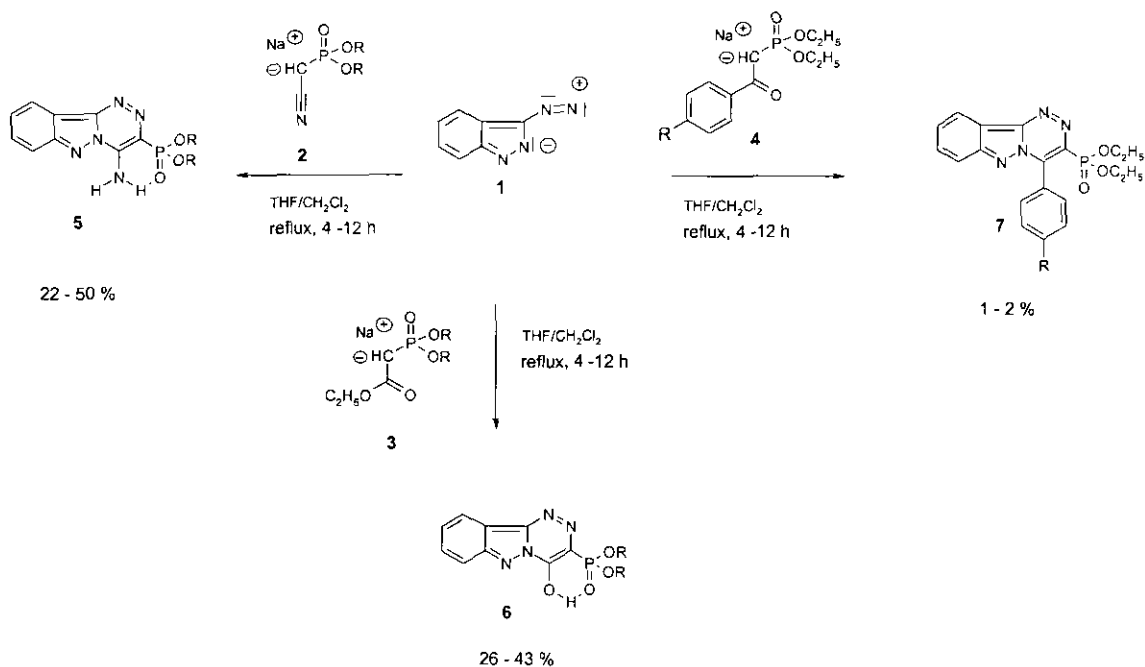


Table 1

5	R
a	CH_3
b	C_2H_5
c	<i>i</i> - C_3H_7

Table 2

6	R
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a C₂H₅
b *i*-C₃H₇

Table 3

7	R
a	H
b	Cl

Scheme 2

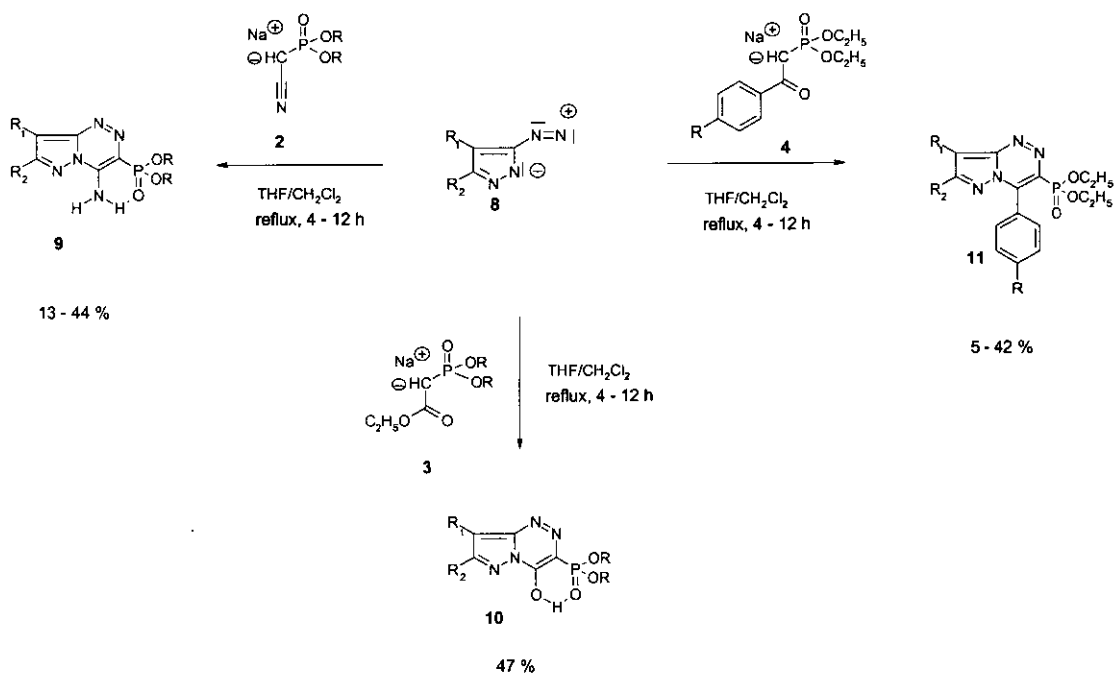


Table 4

9	R ₁	R ₂	R ₃
a	COOC ₂ H ₅	H	C ₂ H ₅
b	COOC ₂ H ₅	H	<i>i</i> -C ₃ H ₇
c	H	CH ₃	C ₂ H ₅
d	H	CH ₃	<i>i</i> -C ₃ H ₇

Table 5

10	R ₁	R ₂	R
	COOC ₂ H ₅	H	C ₂ H ₅

Table 6

11	R ₁	R ₂	R ₃
a	COOC ₂ H ₅	H	H
b	COOC ₂ H ₅	H	CH ₃
c	H	CH ₃	H
d	H	CH ₃	Cl

Scheme 3

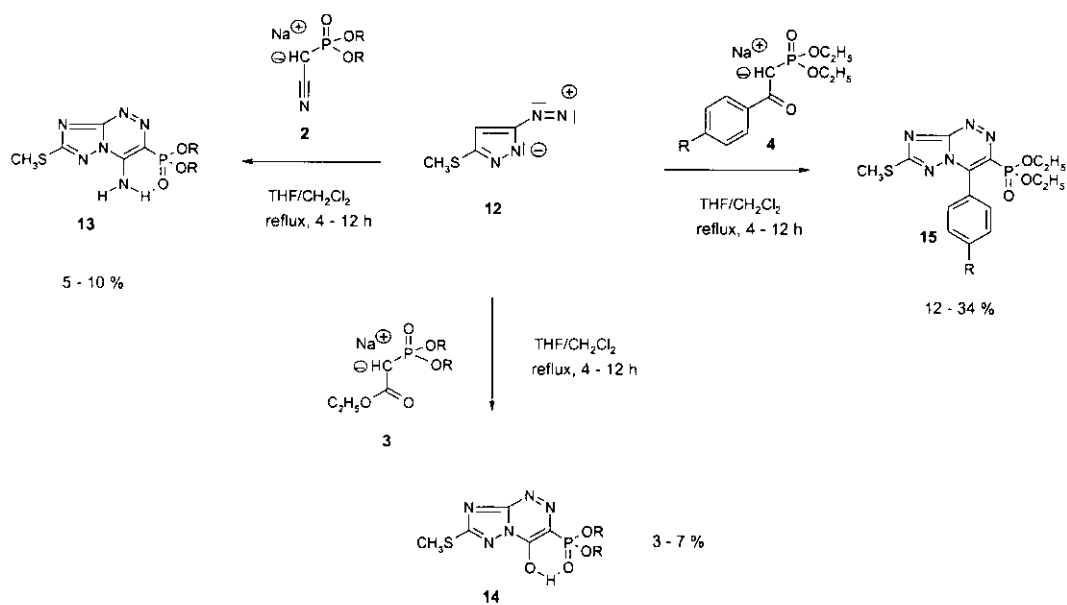


Table 7

13/14	R
a	C ₂ H ₅
b	<i>i</i> -C ₃ H ₇

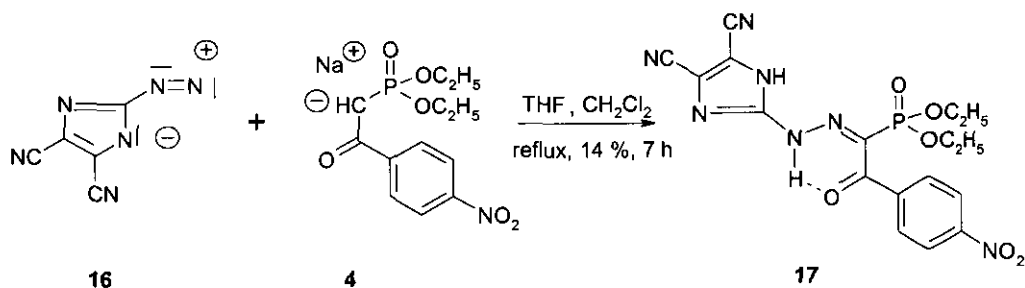
Table 8

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-dicyanoimidazole (**16**), with phosphonate (**4**) and isolated the hydrazone (**17**), which did not cyclize even under strong acidic conditions (Scheme 4).

Scheme 4

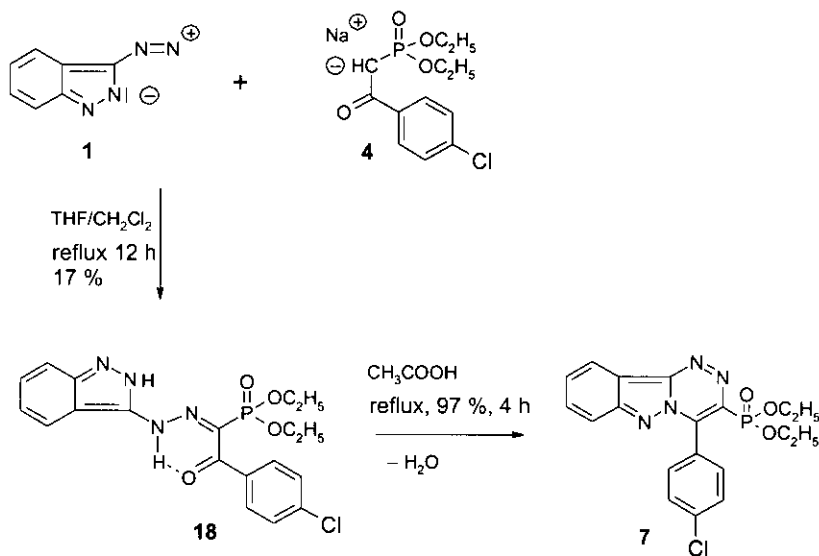


Hydrazone (**18**) was isolable from the reaction of 3-diazoindazole (**1**) with arylmethylphosphonate (**4**) (Scheme 5). By refluxing in acetic acid this hydrazone (**18**) yielded the expected [1,2,4]triazino[4,3-*b*]indazole (**7**) (Scheme 5).

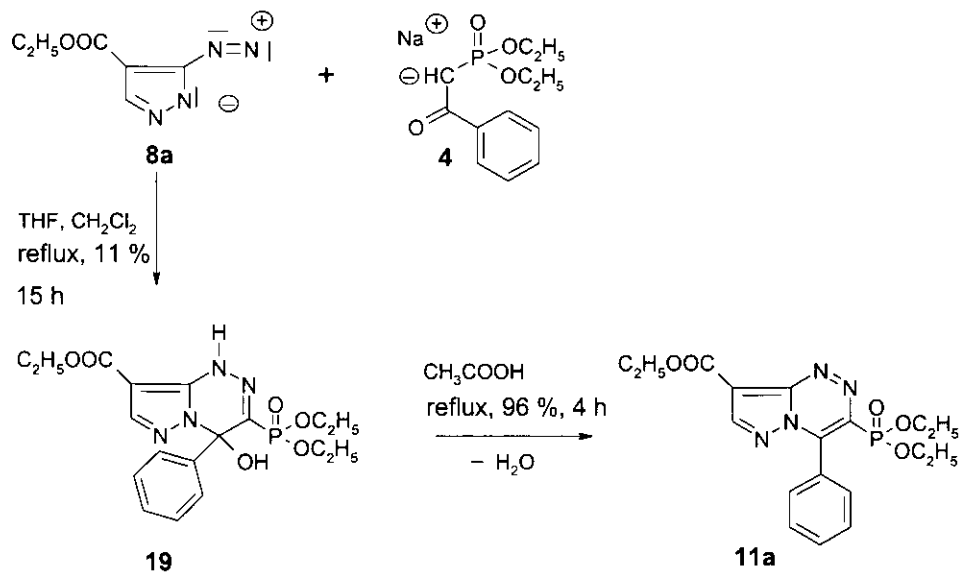
The reaction of 3-diazopyrazol-4-ylcarboxylic acid ethyl ester (**8a**) with benzoylmethylphosphonic acid diethyl ester (**4**) yielded in addition to the expected 3-diethylphosphonatopyrazolo[3,2-*c*][1,2,4]triazin-8-ylcarboxylic acid ethyl ester (**11a**) the dihydro derivative (**19**) (Scheme 6).

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

Scheme 5



Scheme 6



The mechanism of 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, ranging 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 doublets. ^{31}P -NMR spectra proved the phosphonate 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

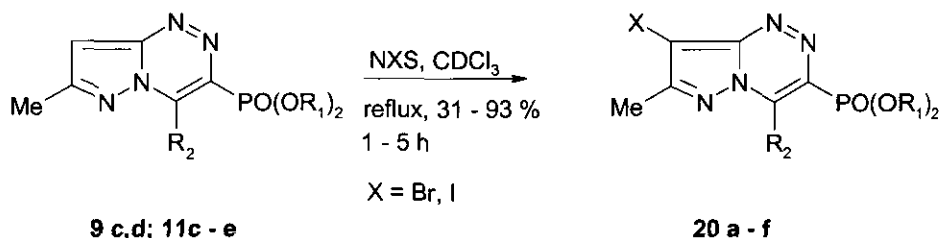


Table 9

20	R ₁	R ₂	X
a	C ₂ H ₅	NH ₂	Br
b	C ₂ H ₅	NH ₂	I
c	C ₂ H ₅	C ₆ H ₅	Br
d	C ₂ H ₅	<i>p</i> -Cl-C ₆ H ₄	Br
e	C ₂ H ₅	C ₆ H ₅	I
f	C ₂ H ₅	<i>p</i> -NO ₂ -C ₆ H ₄	I

g	<i>i</i> -C ₃ H ₇	NH ₂	Br
h	<i>i</i> -C ₃ H ₇	NH ₂	I

It was also intended 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*-Pr)₂NH at 70 to 84°C (reflux) enabled coupling with phenylacetylene to give 7-methyl-8-phenylethynylpyrazolo[3,2-*c*][1,2,4]triazin-3-ylphosphonic acid diethyl esters (**21 a – c**)¹¹ (Scheme 8).

Scheme 8

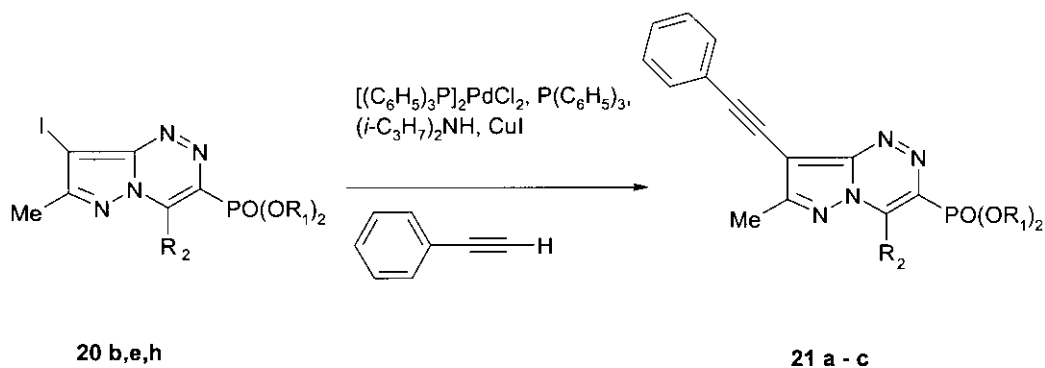


Table 10

21	R ₁	R ₂
a	C ₂ H ₅	NH ₂
b	C ₂ H ₅	C ₆ H ₅
c	<i>i</i> -C ₃ H 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. $(i\text{-Pr})_2\text{NH}$ 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. $^1\text{H-NMR}$ 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. $^{13}\text{C-NMR}$ 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 El.

The syntheses of the phosphonoacetic acid derivatives (**2**) and (**3**) as well as the aroylmethylphosphonic acid diethyl esters (**4**) are described in literature.¹² The diazobetaines were synthesized according to the literature⁸ 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 derivatives (**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), 386sh (4.04). IR: ν = 3338s/3157s (N-H), 2957m, 2853m, 1613s, 1560m, 1528m, 1440s, 1356s, 1250s /1229s (P=O), 1060s/1037s (P-O-C), 970m, 833s, 780s, 754s, 738m, 668m, 627m, 551s, 474s. $^1\text{H-NMR}$ (299.95 MHz, DMSO-d_6): δ = 9.18 (s, 1H, N-H), 8.42 (d, $^3J_{\text{HH}}$ = 8.3 Hz, 1H, arom.H), 8.38 (s, 1H, N-H), 7.94 (d, $^3J_{\text{HH}}$ = 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-CH₃), 3.81 (s, 3H, P-O-CH₃). $^{13}\text{C-NMR}$ (75.43 MHz, DMSO-d_6): δ = 149.91 (s, C-6a), 142.96 (d, $^2J_{\text{CP}}$ = 31.6 Hz, C-4), 130.94 (s, C-8), 122.36 (s, C-10), 120.73 (s, C-9), 118.47 (d, $^1J_{\text{CP}}$ = 232.0 Hz, C-3), 112.62 (s, C-10a), 53.70 (d, $^2J_{\text{CP}}$ = 5.2 Hz, P-O-CH₃). $^{31}\text{P-NMR}$ (121.42 MHz, DMSO-d_6): δ = 13.79 (s). EI-MS : m/z (%) = 294 (15, $[\text{M}+1]^+$), 293 (100, $[\text{M}]^+$), 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. $\text{C}_{11}\text{H}_{12}\text{N}_5\text{O}_3\text{P}$: 293.0677, found: 293.0676. Anal. Calcd for $\text{C}_{11}\text{H}_{12}\text{N}_5\text{O}_3\text{P}$: 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 ($\text{Et}_2\text{O}/\text{CH}_2\text{Cl}_2$ = 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}] = 3353m (NH), 3158m, 2983m, 2344w, 1612s, 1527m, 1357m, 1247s (P=O), 1023s (P-O-C), 971s, 698s. $^1\text{H-NMR}$ (299.95 MHz, CDCl_3): δ [ppm] = 8.69 (1H, N-H), 8.44 (d, 1H, $^3J_{\text{HH}}$ = 8.4 Hz, H-7), 7.80 (d, 1H, $^3J_{\text{HH}}$ = 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-CH₂-CH₃), 1.41 (t, 6H, ³J_{HH} = 7.1 Hz, C-O-CH₂-CH₃). ¹³C-NMR (75.43 MHz, CDCl₃): δ [ppm]= 150.7 (s, C-6a), 143.5 (d, ⁴J_{CP} = 2.1 Hz, 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-CH₂-CH₃), 16.2 (d, ³J_{CP} = 6.6 Hz, C-O-CH₂-CH₃). ³¹P-NMR (121.42 MHz, CDCl₃): δ [ppm]= 11.0 (s). EI-MS : m/z (%) = 322 (18, [M+1]⁺), 321 (100, M)⁺, 248 (26), 213 (48), 185 (87, [M-PO(OC₂H₅)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 C₁₃H₁₆N₅O₃P: 321.0991. Found: 321.0991. Anal. Calcd for C₁₃H₁₆N₅O₃P: 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 (Et₂O/CH₂Cl₂ = 1:1) gave pure **5c** as a yellow solid; yield: 1.32 g (47 %), mp 190 °C. UV/VIS (CH₂Cl₂): λ (log ε) = 228 (4.28), 256 (4.40), 368 (4.19), 388sh (4.11). IR (KBr): ν [cm⁻¹] = 3340m/ 3161m/ 2984m (N-H), 1616s, 1548m, 1441m, 1388m, 1374m, 1357m, 1247s/1229s (P=O), 1177m, 1104m, 1006s (P-O-C), 886m, 779m, 750s, 556s. ¹H-NMR (299.95 MHz, CDCl₃): 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-CH-(CH₃)₂), 1.34 (d, ³J_{HH} = 6.1 Hz, P-O-CH-(CH₃)₂), 1.34 (d, ³J_{HH} = 6.1 Hz, P-O-CH-(CH₃)₂). ¹³C-NMR (62.89 MHz, CDCl₃): 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-CH-(CH₃)₂), 23.97-23.74 (m, P-O-CH-(CH₃)₂). ³¹P-NMR (121.42 MHz, CDCl₃): δ [ppm]= 9.12 (s). EI-MS : m/z (%) = 350 (7, [M+1]⁺), 349 (38, [M]⁺), 307 (10, [M-C₃H₆]⁺), 266 (13), 265 (100, [M-2 C₃H₇O]⁺), 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 C₁₅H₂₀N₅O₃P: 349.1305. Found: 349.1306. Anal. Calcd for C₁₅H₂₀N₅O₃P: 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 (Et₂O/CH₂Cl₂ = 1:1) gave pure **6a** as an orange solid; yield: 688 mg (42%), mp 189-191 °C. UV/VIS (CH₂Cl₂): λ (log ε) = 230 (4.11), 270 (4.36), 280 (4.33), 340sh (3.95), 354 (3.98), 402 (3.72). IR (KBr): ν [cm⁻¹] = 3430w, 2763m, 1700s, 1638m, 1465s, 1259m (P=O), 1236m, 1052s, 1022s (P-O-C), 752s, 568s. ¹H-NMR (299.95 MHz, CDCl₃): 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-CH₂-CH₃), 1.46 (t, ³J_{HH} = 7.0 Hz, 6H, P-O-CH₂-CH₃). ¹³C-NMR (75.43 MHz, CDCl₃): 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-CH₂-CH₃), 16.36 (d, ³J_{CP} = 6.5 Hz, P-O-CH₂-CH₃). ³¹P-NMR (121.42 MHz, CDCl₃): 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: C₁₃H₁₅N₄O₄P: 322.0832. Found: 322.0833. Anal. Calcd for C₁₃H₁₅N₄O₄P: 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 (CH₂Cl₂): λ (log ε) = 228 (4.16), 270 (4.12), 280 (4.05), 352 (4.04), 396 (3.76). IR (KBr): ν [cm⁻¹] = 3389w, 2982s, 1702s, 1638s, 1470s, 1375m, 1242s (P=O), 1023s (P-O-C), 982s, 750s. ¹H-NMR (250.13 MHz, CDCl₃): 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-CH(CH₃)₂), 1.48 (d, 6H, ³J_{HH} = 6.2 Hz, P-O-CH(CH₃)₂), 1.41 (d, 6H, ³J_{HH} = 6.2 Hz, P-O-CH(CH₃)₂). ¹³C-NMR (90.56 MHz, CDCl₃): 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-CH-(CH₃)₂), 24.10-24.00 (m, P-O-CH-(CH₃)₂). $^{31}\text{P-NMR}$ (121.42 MHz, CDCl₃): 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-2C₃H₇]⁺), 238 (39, [M-2C₃H₇-N₂]⁺), 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 C₁₅H₁₉N₄O₄P: 350.1145. Found: 350.1146. Anal. Calcd for C₁₅H₁₉N₄O₄P: 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 (CH₂Cl₂): λ (log ϵ) = 230 (4.21), 294 (3.90), 352 (4.07). IR: ν = 3365s (N-H), 3275m, 3227m, 2984m, 1685s (C=O), 1629s, 1565s, 1497s, 1440m, 1288m, 1226s (P=O), 1141m, 1027s (P-O-C), 971m, 782s, 576s, 517s. $^1\text{H-NMR}$ (250.13 MHz, CDCl₃): 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-CH₂-CH₃), 4.37-4.20 (m, 4H, P-O-CH₂-CH₃), 1.46 (t, 3H, $^3J_{HH} = 7.1$ Hz, C-O-CH₂-CH₃), 1.40-1.35 (m, 6H, P-O-CH₂-CH₃). $^{13}\text{C-NMR}$ (62.89 MHz, CDCl₃): 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-CH₂-CH₃), 61.08 (s, C-O-CH₂-CH₃), 16.19 (d, $^3J_{CP} = 6.5$ Hz, P-O-CH₂-CH₃), 14.52 (s, C-O-CH₂-CH₃). $^{31}\text{P-NMR}$ (121.42 MHz, CDCl₃): δ = 9.83 (s). EI-MS : m/z (%) = 343 (35, [M]⁺), 299 (41), 298 (14, [M-C₂H₅O]⁺), 271 (67), 270 (100, [M-COOC₂H₅]⁺), 243 (19), 242 (16), 236 (10), 235 (76), 234 (24), 224 (12), 215 (13), 207 (25, [M-PO(OC₂H₅)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 C₁₂H₁₈N₅O₅P: 343.1047, Found: 343.1048. Anal. Calcd for C₁₂H₁₈N₅O₅P: 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}] = 3366m (N-H), 3275m, 3224m, 2983m, 1692s (C=O), 1628s, 1566s, 1497m, 1437m, 1386m, 1223m, 1185s (P=O), 1006m (P-O-C), 783m, 579m, 528m. $^1\text{H-NMR}$ (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-CH-(CH_3)₂), 4.50 (q, 2H, $^3\text{J}_{\text{HH}} = 7.1$ Hz, C-O-CH₂-CH₃), 1.45 (t, 3H, $^3\text{J}_{\text{HH}} = 7.1$ Hz, C-O-CH₂-CH₃), 1.38 (d, 6H, $^3\text{J}_{\text{HH}} = 6.1$ Hz, P-O-CH-(CH_3)₂), 1.33 (d, 6H, $^3\text{J}_{\text{HH}} = 6.3$ Hz, P-O-CH-(CH_3)₂). $^{13}\text{C-NMR}$ (75.43 MHz, CDCl_3): δ [ppm]= 161.70 (s, C=O), 148.16 (s, C-7), 146.52 (d, $^4\text{J}_{\text{CP}} = 2.0$ Hz, C-8a), 142.57 (d, $^2\text{J}_{\text{CP}} = 31.3$ Hz, C-4), 120.97 (d, $^1\text{J}_{\text{CP}} = 234.8$ Hz, C-3), 104.57 (s, C-8), 73.49 (d, $^2\text{J}_{\text{CP}} = 6.5$ Hz, P-O-CH-(CH_3)₂), 60.97 (s, C-O-CH₂-CH₃), 23.94-23.74 (m, P-O-CH-(CH_3)₂), 14.50 (s, C-O-CH₂-CH₃). $^{31}\text{P-NMR}$ (121.42 MHz, CDCl_3): δ [ppm]= 8.01 (s). EI-MS : m/z (%) = 371 (16, $[\text{M}]^+$), 314 (11), 313 (42, $[\text{M}-\text{C}_3\text{H}_6\text{O}]^+$), 271 (43, $[\text{M}-\text{C}_3\text{H}_6\text{O}-\text{C}_3\text{H}_7]^+$), 270 (32), 242 (13), 216 (22), 215 (100), 108 (12), 95 (10), 42 (35), 40 (13). HR-MS m/z Calcd for $\text{C}_{14}\text{H}_{22}\text{N}_5\text{O}_5\text{P}$: 371.1357. Found: 371.1355. Anal. Calcd for $\text{C}_{14}\text{H}_{22}\text{N}_5\text{O}_5\text{P}$: 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 = 3336m / 3141s (N-H), 2983m, 1628s, 1572s, 1390m, 1272m, 1245m, 1213s (P=O), 1080m, 1040s (P-O-C), 973m, 959m, 799m, 751m, 657m, 627m, 579m, 518m. $^1\text{H-NMR}$ (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-CH₂-CH₃), 2.56 (s, 3H, CH_3 at C-7), 1.37 (dt, 6H, $^3\text{J}_{\text{HH}} = 7.1$ Hz, $^4\text{J}_{\text{HP}} = 0.7$ Hz, P-O-CH₂-CH₃). $^{13}\text{C-NMR}$ (75.43 MHz, CDCl_3): δ = 156.54 (C-7), 149.39 (d, $^4\text{J}_{\text{CP}} = 2.0$ Hz, C-8a), 142.57 (d, $^2\text{J}_{\text{CP}} = 31.0$ Hz, C-4), 115.66 (d, $^1\text{J}_{\text{CP}} = 236.9$ Hz, C-3),

97.97 (s, C-8), 63.73 (d, $^2J_{CP} = 5.9$ Hz, P-O-CH₂-CH₃), 16.20 (d, $^3J_{CP} = 6.8$ Hz, P-O-CH₂-CH₃), 14.54 (s, CH₃ at C-7). $^{31}\text{P-NMR}$ (121.42 MHz, CDCl₃): $\delta = 12.65$ (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 C₁₀H₁₆N₅O₃P: 285.0991. Found: 285.0991. Anal. Calcd for C₁₀H₁₆N₅O₃P: 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 CH₂Cl₂ with n-hexane gave pure **10** as a yellow solid; yield: 1.61 g (46 %), mp 140 °C. UV/VIS (CH₂Cl₂): λ (log ϵ) = 230 (4.03), 260 (4.36), 330 (4.25). IR (KBr): ν [cm⁻¹] = 3001m, 1731s, 1709s, 1600s, 1517s, 1242s (P=O), 1128s, 1022s (P-O-C), 776m. $^1\text{H-NMR}$ (250.13 MHz, CDCl₃): δ [ppm] = 8.28 (s, H-7), 4.44-4.32 (m, 6H, C-O-CH₂-CH₃, P-O-CH₂-CH₃), 1.42-1.37 (m, 9H, C-O-CH₂-CH₃, P-O-CH₂-CH₃). $^{13}\text{C-NMR}$ (62.89 MHz, CDCl₃): 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-CH₂-CH₃), 61.36 (s, C-O-CH₂-CH₃), 16.40 (d, $^3J_{CP} = 6.2$ Hz, P-O-CH₂-CH₃), 14.41 (s, C-O-CH₂-CH₃). $^{31}\text{P-NMR}$ (121.42 MHz, CDCl₃): δ [ppm] = 5.35 (s). EI-MS : m/z (%) = 372 (26, [M+28]⁺), 344 (29, M⁺), 299 (17, [M-C₂H₅O]⁺), 298 (33, [M-C₂H₆O]⁺), 271 (16), 264 (20), 263 (59), 236 (37), 235 (47), 190 (56), 189 (79), 163 (22), 162 (29, [M-C₂H₆O-PO(OC₂H₅)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 C₁₂H₁₇N₄O₆P: 344.0887. Found: 344.0888. Anal. Calcd for C₁₂H₁₇N₄O₆P: 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 (CH₂Cl₂): λ (log ϵ) = 228 (3.67), 254 (3.96), 308 (3.34). IR: ν =

3421m, 2772s, 1724m, 1616s, 1507s, 1430m, 1376m, 1274s, 1237s (P=O), 1208m, 1160m, 1074s, 1021s (P-O-C), 758m, 533m. $^1\text{H-NMR}$ (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-CH₂-CH₃), 2.75 (s, 3H, S-CH₃), 1.38 (dt, 6H, $^3J_{\text{HH}}$ = 7.1 Hz, $^4J_{\text{HP}}$ = 0.8 Hz, P-O-CH₂-CH₃). $^{13}\text{C-NMR}$ (75.43 MHz, CDCl_3): δ = 171.16 (s, C-7), 155.50 (d, $^4J_{\text{CP}}$ = 1.9 Hz, C-8a), 142.22 (d, $^3J_{\text{CP}}$ = 32.1 Hz, C-4), 121.68 (d, $^2J_{\text{CP}}$ = 235.2 Hz, C-3), 64.44 (d, $^2J_{\text{CP}}$ = 6.2 Hz, P-O-CH₂-CH₃), 16.17 (d, $^3J_{\text{CP}}$ = 6.5 Hz, P-O-CH₂-CH₃), 14.10 (s, S-CH₃). $^{31}\text{P-NMR}$ (121.42 MHz, CDCl_3): δ = 9.69 (s). EI-MS : m/z (%) = 318 (20, $[\text{M}]^+$), 274 (73), 246 (13), 245 (96), 211 (12), 210 (100), 209 (16), 199 (13), 182 (25, $[\text{M-PO}(\text{OC}_2\text{H}_5)_2+\text{H}]^+$), 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 $\text{C}_9\text{H}_{15}\text{N}_6\text{O}_3\text{PS}$: 318.0064. Found: 318.0064. Anal. Calcd for $\text{C}_9\text{H}_{15}\text{N}_6\text{O}_3\text{PS}$: 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 / Et₂O = 5:2), stirring in Et₂O for 24 h and recrystallisation from Et₂O gave pure **13b** as a light brown solid; yield: 180 mg (5 %), mp 124 °C. UV/VIS (CH_2Cl_2): λ (log ϵ) = 230sh (3.82), 254 (4.42), 318 (3.83). IR (KBr): ν [cm^{-1}] = 3080s, 2908s, 2750s, 1629s, 1523m, 1450s, 1288s (P=O), 1102w, 1030s (P-O-C), 999s, 857w, 709s, 581w. $^1\text{H-NMR}$ (299.95 MHz, acetone-d₆): δ [ppm] = 8.80 (s, 1H, N-H), 8.31 (s, 1H, N-H), 4.89-4.76 (m, 2H, P-O-CH-(CH₃)₂), 2.72 (s, 3H, S-CH₃), 1.36 (d, 6H, $^3J_{\text{HH}}$ = 6.2 Hz, P-O-CH-(CH₃)₂), 1.28 (d, 6H, $^3J_{\text{HH}}$ = 6.1 Hz, P-O-CH-(CH₃)₂). $^{13}\text{C-NMR}$ (62.89 MHz, acetone-d₆): δ [ppm] = 170.67 (s, C-7), 157.01 (s, C-8a), 144.20 (d, $^2J_{\text{CP}}$ = 33.8 Hz, C-4), 123.73 (d, $^1J_{\text{CP}}$ = 234.3 Hz, C-3), 73.32 (d, $^2J_{\text{CP}}$ = 5.2 Hz, P-O-CH-(CH₃)₂), 24.14-23.87 (m, P-O-CH-(CH₃)₂), 13.90 (s, S-CH₃). $^{31}\text{P-NMR}$ (121.42 MHz, acetone-d₆): δ [ppm] = 7.23 (s). EI-MS : m/z (%) = 347 (5, $[\text{M}+1]^+$), 346 (33, $[\text{M}]^+$), 289 (19), 288 (73, $[\text{M-C}_3\text{H}_6\text{O}]^+$), 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 $\text{C}_{11}\text{H}_{19}\text{N}_6\text{O}_3\text{PS}$: 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}] = 3420m (O-H), 3231w, 3126w, 2982s / 2930s (S-CH₃), 2772s, 1724s, 1610s, 1507s, 1376m, 1273s (P=O), 1237s, 1209m, 1161m, 1073s (P-O-C), 1021s, 985m, 933m, 758s, 553s, 481m. ¹H-NMR (299.95 MHz, $CDCl_3$): δ [ppm] = 4.46-4.29 (m, 4H, P-O-CH₂-CH₃), 2.69 (s, 3H, S-CH₃), 1.40 (dt, 6H, ³J_{HH} = 7.1 Hz, ⁴J_{HP} = 0.7 Hz, P-O-CH₂-CH₃). ¹³C-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-CH₂-CH₃), 16.28 (d, ³J_{CP} = 6.5 Hz, P-O-CH₂-CH₃), 14.05 (s, S-CH₃). ³¹P-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}] = 3420m, 2981s (O-H), 2932m, 2747m, 1729s, 1599s, 1510s, 1435s, 1375s, 1269s, 1236s (P=O), 1207m, 1168m, 1100m, 1002s (P-O-C), 934m, 888m, 767m, 603m, 568s. ¹H-NMR (299.95 MHz, acetone-d₆): δ [ppm] = 4.73 (q, 2H, ³J_{HH} = 6.4 Hz, P-O-CH(CH₃)₂), 2.67 (s, 3H, S-CH₃), 1.18 (m, 12H, P-O-CH-

(CH₃)₂). ¹³C-NMR (75.43 MHz, acetone-d₆): 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-(CH₃)₂), 24.12-23.79 (m, P-O-CH-(CH₃)₂), 14.01 (s, S-CH₃). ³¹P-NMR (121.42 MHz, acetone-d₆): 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 C₁₁H₁₈N₅O₄PS: 347.0817. Found: 347.0817. Anal. Calcd for C₁₁H₁₈N₅O₄PS: 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 (MgSO₄), 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 Et₂O gave pure **7a** as an orange solid; yield: 85 mg (2 %), mp 146-147 °C. UV/VIS (CH₂Cl₂): 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. ¹H-NMR (299.95 MHz, CDCl₃): δ [ppm]= 7.85-6.76 (m, 9H, arom. C-H), 4.38-4.29 (m, 4H, P-O-CH₂-CH₃), 1.39 (t, 6H, ³J_{HH} = 6.9 Hz, P-O-CH₂-CH₃). ¹³C-NMR (90.56 MHz, CDCl₃): 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-CH₂-CH₃), 16.17 (d, ³J_{CP} = 6.9 Hz, P-O-CH₂-CH₃). 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 . 1H -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- CH_2 - CH_3), 1.31-1.26 (m, 6H, P-O- CH_2 - CH_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- CH_2 - CH_3), 16.20 (d, $^3J_{CP}$ = 7.0 Hz, P-O- CH_2 - CH_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 a 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), 308sh (3.70), 356 (3.61), 390sh (3.52). IR: ν = 3431m, 2979m, 1726s (C=O), 1576s, 1476s, 1340s, 1273s, 1201s (P=O), 1142s, 1051s/1019s (P-O-C), 982m, 751m, 702m, 531s. $^1\text{H-NMR}$ (299.95 MHz, CDCl_3): δ = 8.72 (s, 1H, H-7), 7.81-7.63 (m, 5H, arom. H), 4.55 (q, 2H, $^3J_{\text{HH}} = 7.1$ Hz, C-O- CH_2 - CH_3), 4.31-4.07 (m, 4H, P-O- CH_2 - CH_3), 1.48 (t, 3H, $^3J_{\text{HH}} = 7.1$ Hz, C-O- CH_2 - CH_3), 1.22 (t, 6H, $^3J_{\text{HH}} = 7.1$ Hz, P-O- CH_2 - CH_3). $^{13}\text{C-NMR}$ (90.56 MHz, CDCl_3): δ = 161.36 (s, C=O), 149.45 (s, C-7), 147.78 (s, C-8a), 140.03 (d, $^2J_{\text{CP}} = 28.9$ Hz, C-4), 138.15 (d, $^1J_{\text{CP}} = 235.0$ 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, $^2J_{\text{CP}} = 6.3$ Hz, P-O- CH_2 - CH_3), 61.38 (s, C-O- CH_2 - CH_3), 16.14 (d, $^3J_{\text{CP}} = 6.7$ Hz, P-O- CH_2 - CH_3), 14.51 (s, C-O- CH_2 - CH_3). $^{31}\text{P-NMR}$ (121.42 MHz, CDCl_3): δ = 7.86 (s) EI-MS : m/z (%) = 406 (3), 405 (20, $[\text{M}+1]^+$), 404 (100, $[\text{M}]^+$), 375 (11, $[\text{M}-\text{C}_2\text{H}_5]^+$), 360 (37), 359 (35, $[\text{M}-\text{C}_2\text{H}_5\text{O}]^+$), 358 (29), 331 (33, $[\text{M}-\text{COOC}_2\text{H}_5]^+$), 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 $\text{C}_{18}\text{H}_{21}\text{N}_4\text{O}_5\text{P}$: 404.1248. Found: 404.1246. Anal. Calcd for $\text{C}_{18}\text{H}_{21}\text{N}_4\text{O}_5\text{P}$: 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), 378sh (3.75). IR (KBr): ν [cm^{-1}] = 3447m, 2988m (arom. H), 1703s (C=O), 1611w, 1566m, 1522m, 1487s, 1436m, 1373w, 1276s, 1252s/1207s (P=O), 1140s, 1052s/1022s (P-O-C), 939m, 786k, 753m, 589s, 552s, 459w. $^1\text{H-NMR}$ (250.13 MHz, CDCl_3): δ [ppm] = 8.71 (s, 1H, H-7), 7.70 (d, 2H, $^3J_{\text{HH}} = 8.0$ Hz, C-H), 7.43 (d, 2H, $^3J_{\text{HH}} = 8.0$ Hz, C-H), 4.54 (q, 2H, $^3J_{\text{HH}} = 7.1$ Hz, C-O- CH_2 - CH_3), 4.29-4.13 (m, 4H, P-O- CH_2 - CH_3), 2.49 (s, 3H, C_6H_4 - CH_3), 1.48 (t, 3H, $^3J_{\text{HH}} = 7.1$ Hz, C-O- CH_2 - CH_3), 1.24 (t, 6H, $^3J_{\text{HH}} = 7.0$ Hz, P-

O-CH₂-CH₃). ¹³C-NMR (62.89 MHz, CDCl₃): 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-CH₂-CH₃), 61.34 (s, C-O-CH₂-CH₃), 21.76 (s, arom. CH₃), 16.14 (d, ³J_{CP} = 6.3 Hz, P-O-CH₂-CH₃), 14.51 (s, C-O-CH₂-CH₃). ³¹P-NMR (121.42 MHz, CDCl₃): δ [ppm]= 19.37 (s). EI-MS : m/z (%) = 420 (4), 419 (22, [M+1]⁺), 418 (100, [M]⁺), 374 (15), 373 (22, [M-C₂H₅O]⁺), 372 (26), 359 (52), 345 (22, [M-COOC₂H₅]⁺), 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 C₁₉H₂₃N₄O₅P: 418.1407. Found: 418.1408. Anal. Calcd for C₁₉H₂₃N₄O₅P: 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 Et₂O gave pure **11c** as a yellow solid; yield: 2.17 g (41 %), mp 120-121 °C. UV/VIS (CH₂Cl₂): λ (log ε) = 244 (4.44), 286sh (3.74), 366 (3.50). IR (KBr): ν [cm⁻¹] = 3419s, 2986m, 1558m, 1514w, 1468s, 1444w, 1286m, 1244s (P=O), 1217m, 1161m, 1057s, 1025s (P-O-C), 983m, 952m, 776m, 750m, 693s, 585s, 510m, 453m. ¹H-NMR (250.13 MHz, CDCl₃): 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-CH₂-CH₃), 2.56 (s, 3H, CH₃), 1.21 (t, 6H, ³J_{HH} = 7.1 Hz, P-O-CH₂-CH₃). ¹³C-NMR (90.56 MHz, CDCl₃): 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-CH₂-CH₃), 16.14 (d, ³J_{CP} = 6.5 Hz, P-O-CH₂-CH₃), 14.92 (s, CH₃). EI-MS : m/z (%) = 347 (19, [M+1]⁺), 346 (100, [M]⁺), 302 (32), 301 (30, [M-C₂H₅O]⁺), 273 (41, [M-C₂H₅O-C₂H₄]⁺), 238 (42), 237 (60), 211 (19), 210 (82), 209 (60, [M-PO-(OC₂H₅)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, [C₆H₅]⁺), 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. 1H -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-CH₂-CH₃), 2.57 (s, 3H, CH₃), 1.26 (t, 6H, $^3J_{HH} = 7.1$ Hz, P-O-CH₂-CH₃). ^{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-CH₂-CH₃), 16.16 (d, $^3J_{CP} = 6.4$ Hz, P-O-CH₂-CH₃), 14.86 (s, CH₃). ^{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 = 3448s (O-H), 2980m, 1540m, 1517m, 1481m, 1352s, 1313s, 1275s / 1250s (P=O), 1113m,

1058s / 1025s (P-O-C), 989m, 962m, 783m, 711m, 640m, 568m. $^1\text{H-NMR}$ (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-CH₂-CH₃), 2.73 (s, 3H, S-CH₃), 1.21 (t, 6H, $^3\text{J}_{\text{HH}} = 7.2$ Hz, P-O-CH₂-CH₃). $^{13}\text{C-NMR}$ (75.43 MHz, CDCl_3): δ = 174.00 (s, C-7), 156.28 (d, $^4\text{J}_{\text{CP}} = 2.6$ Hz, C-8a), 139.13 (d, $^2\text{J}_{\text{CP}} = 30.4$ Hz, C-4), 138.99 (d, $^1\text{J}_{\text{CP}} = 237.0$ 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, $^2\text{J}_{\text{CP}} = 6.5$ Hz, P-O-CH₂-CH₃), 16.07 (d, $^3\text{J}_{\text{CP}} = 6.4$ Hz, P-O-CH₂-CH₃), 14.10 (s, S-CH₃). $^{31}\text{P-NMR}$ (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-C₂H₅O]⁺), 332 (13), 306 (31, [M-C₂H₅O-C₂H₄]⁺), 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 C₁₅H₁₈N₅O₃PS: 379.0867. Found: 379.0867. Anal. Calcd for C₁₅H₁₈N₅O₃PS: 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 Et₂O 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. $^1\text{H-NMR}$ (299.95 MHz, CDCl_3): δ [ppm] = 7.78 (d, 2H, $^3\text{J}_{\text{HH}} = 8.1$ Hz, H-2', H-6'), 7.42 (d, 2H, $^3\text{J}_{\text{HH}} = 8.1$ Hz, H-3', H-5'), 4.28-4.11 (m, 4H, P-O-CH₂-CH₃), 2.74 (s, 3H, S-CH₃), 2.49 (s, 3H, arom. CH₃), 1.23 (t, $^3\text{J}_{\text{HH}} = 7.1$ Hz, P-O-CH₂-CH₃). $^{13}\text{C-NMR}$ (62.89 MHz, CDCl_3): δ [ppm] = 156.56 (s, C-7), 143.03 (s, C-8a), 139.75 (d, $^2\text{J}_{\text{CP}} = 30.6$ Hz, C-4), 139.16 (d, $^1\text{J}_{\text{CP}} = 236.3$ 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, $^2\text{J}_{\text{CP}} = 6.2$ Hz, P-O-CH₂-CH₃), 21.79 (s, arom. CH₃), 16.09 (d, $^3\text{J}_{\text{CP}} = 7.0$ Hz, P-O-CH₂-CH₃), 14.11 (s, S-CH₃). $^{31}\text{P-NMR}$ (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 = 3289s (N-H), 2983m, 1636s (C=O), 1590m, 1559s, 1437m, 1398s, 1294s, 1262s (P=O), 1173m, 1092m, 1020s (P-O-C), 983s, 869m, 804m, 762m, 745m, 589m. 1H -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-CH₂-CH₃), 1.43-1.23 (m, 6H, P-O-CH₂-CH₃). ^{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-CH₂-CH₃), 16.38-16.14 (m, P-O-CH₂-CH₃). 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 = 3303s/3144s (NH,OH), 2982m, 1666s (C=O), 1603s, 1545s, 1287m, 1228s (P=O), 1162m, 1127m,

1048s/1024s (P-O-C), 781m, 700m, 581m, 560m. $^1\text{H-NMR}$ (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-CH₂-CH₃), 3.92-3.78 (m, 4H, P-O-CH₂-CH₃), 1.29 (m, 3H, C-O-CH₂-CH₃), 1.09-1.06 (m, 6H, P-O-CH₂-CH₃). $^{13}\text{C-NMR}$ (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, $^1J_{\text{CP}}$ = 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, $^2J_{\text{CP}}$ = 26.1 Hz, C-4), 61.82 (d, $^2J_{\text{CP}}$ = 5.5 Hz, P-O-CH₂-CH₃), 59.39 (s, C-O-CH₂-CH₃), 15.84 (d, $^3J_{\text{CP}}$ = 6.9 Hz, P-O-CH₂-CH₃), 14.22 (s, C-O-CH₂-CH₃). EI-MS : m/z (%) = 423 (3, $[\text{M}+1]^+$), 422 (15, $[\text{M}]^+$), 404 (4, $[\text{M}-\text{H}_2\text{O}]^+$), 345 (9, $[\text{M}-\text{C}_6\text{H}_5]^+$), 285 (18, $[\text{M}-\text{PO}(\text{OC}_2\text{H}_5)_2]^+$), 271 (9), 239 (4, $[\text{M}-\text{PO}(\text{OC}_2\text{H}_5)-\text{C}_2\text{H}_6\text{O}]^+$), 185 (13), 108 (12), 105 (100, $[\text{C}_7\text{H}_5\text{O}]^+$), 77 (19, $[\text{C}_6\text{H}_5]^+$). HR-MS: m/z Calcd for $\text{C}_{18}\text{H}_{23}\text{N}_4\text{O}_6\text{P}$: 422.1353. Found: 422.1351. Anal. Calcd for $\text{C}_{18}\text{H}_{23}\text{N}_4\text{O}_6\text{P}$: 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 = 3269s (N-H), 2989m, 1625s, 1560s, 1465m, 1390m, 1218s (P=O), 1171m, 1080m, 1026s (P-O-C), 978m, 861m, 797m, 761s, 621m, 568s, 497s.

$^1\text{H-NMR}$ (250.13 MHz, CDCl_3): δ = 8.59 (1H, N-H), 6.98 (1H, N-H), 4.40-4.18 (m, 4H, P-O-CH₂-CH₃), 2.52 (s, 3H, CH₃), 1.37 (t, 6H, $^3J_{\text{HH}}$ = 6.9 Hz, P-O-CH₂-CH₃). $^{13}\text{C-NMR}$ (62.89 MHz, CDCl_3): δ = 155.41 (s, C-7), 145.88 (s, C-8a), 142.63 (d, $^2J_{\text{CP}}$ = 31.7 Hz, C-4), 117.18 (d, $^1J_{\text{CP}}$ = 236.6 Hz, C-3), 86.66 (s, C-8), 64.15 (d, $^2J_{\text{CP}}$ = 6.1 Hz, P-O-CH₂-CH₃), 16.21 (d, $^3J_{\text{CP}}$ = 6.2 Hz, P-O-CH₂-CH₃), 13.12 (s, CH₃ at C-7). EI-MS : m/z (%) = 366 (8), 365 (66, $[\text{Br}]^+$).

M]⁺), 364 (11), 363 (67, [⁷⁹Br-M]⁺), 321 (40 [⁸¹Br-M-C₂H₄O]⁺), 319 (44, [⁷⁹Br-M-C₂H₄O]⁺), 293 (10), 292 (71, [⁸¹Br-M-C₂H₄O-C₂H₅]⁺), 291 (18), 290 (69), [⁷⁹Br-M-C₂H₄O-C₂H₅]⁺, 289 (10), 257 (80), 256 (42), 255 (82), 254 (32), 230 (10), 229 (100, [⁸¹Br-M-PO(OC₂H₅)₂+H]⁺), 228 (16), 227 (96, [⁷⁹Br-M-PO(OC₂H₅)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 C₁₀H₁₅N₅O₃⁷⁹BrP: 363.0096. Found: 363.0096. Anal. Calcd for C₁₀H₁₅N₅O₃⁷⁹BrP: 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 (CH₂Cl₂): λ (log ε) = 230sh (4.08), 252 (4.52), 286 (3.69), 392 (3.44). IR (KBr): ν [cm⁻¹] = 3448m, 3162m, 3058m, 2926s, 2855m, 1772m, 1700s, 1511m, 1465m, 1375m, 1288m, 1251s (P=O), 1229m, 1178s, 1121w, 1050s, 1022s (P-O-C), 962m, 822m, 796m, 777m, 694m, 651m, 588m, 540m. ¹H-NMR (250.13 MHz, CDCl₃): 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-CH₂-CH₃), 2.54 (s, 3H, CH₃ at C-7), 1.21 (t, 6H, ³J_{HH} = 7.1 Hz, P-O-CH₂-CH₃). ¹³C-NMR (90.56 MHz, CDCl₃): 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-CH₂-CH₃), 16.09 (d, ³J_{CP} = 7.2 Hz, P-O-CH₂-CH₃), 13.41 (s, CH₃ at C7). EI-MS : m/z (%) = 427 (16), 426 (82, [⁸¹Br-M]⁺), 25 (15), 424 (100, [⁷⁹Br-M]⁺), 382 (35, [⁸¹Br-M-C₂H₄O]⁺), 381 (25), 380 (35, [⁷⁹Br-M-C₂H₄O]⁺), 379 (19), 353 (33, [⁸¹Br-M-C₂H₄O-C₂H₅]⁺), 351 (38, [⁷⁹Br-M-C₂H₄O-C₂H₅]⁺), 318 (32), 317 (59), 316 (36), 315 (52), 289 (37, [⁸¹Br-M-PO(OC₂H₅)₂]⁺), 287 (31, [⁷⁹Br-M-PO(OC₂H₅)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, [⁸¹Br]⁺), 79 (11, [⁷⁹Br]⁺), 65 (12). HR-MS: m/z Calcd for C₁₆H₁₈N₄O₃⁷⁹BrP: 424.0299. Found: 424.0298. Anal. Calcd for C₁₆H₁₈N₄O₃⁷⁹BrP: 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 Et₂O for 12 h gave pure **20d** as yellow needles; yield: 135 mg (93 %), mp 120 °C. UV/VIS (CH₂Cl₂): λ (log ε) = 228sh (4.07), 252 (4.51), 294 (3.79), 392 (3.45). IR (KBr): ν [cm⁻¹] = 3448m, 3088w, 2985m (arom. H), 1596m, 1533m, 1513m, 1480s, 1404w, 1388w, 1286m, 1255s (P=O), 1221m, 1171m, 1159w, 1095m, 1053s, 1009s (P-O-C), 978s, 837m, 801m, 773m, 588s, 547s, 509m. ¹H-NMR (250.13 MHz, CDCl₃): 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-CH₂-CH₃), 2.55 (s, 3H, CH₃), 1.25 (t, 6H, ³J_{HH} = 7.0 Hz, P-O-CH₂-CH₃). ¹³C-NMR (90.56 MHz, CDCl₃): 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-CH₂-CH₃), 16.16 (d, ³J_{CP} = 6.4 Hz, P-O-CH₂-CH₃), 13.37 (s, CH₃ at C-7). EI-MS : m/z (%) = 463 (5), 462 (24, [⁸¹Br-³⁷Cl-M]⁺), 461 (17), 460 (100, [⁸¹Br-³⁵Cl-M/⁷⁹Br-³⁷Cl-M]⁺), 459 (18), 458 (76, [⁷⁹Br-³⁵Cl-M]⁺), 432 (13), 418 (11), 417 (13), 416 (55, [⁸¹Br-³⁵Cl-M-C₂H₄O/⁷⁹Br-³⁷Cl-M-C₂H₄O]⁺), 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 C₁₆H₁₇N₄O₃⁷⁹Br³⁵ClP: 457.9910. Found: 457.9910. Anal. Calcd for C₁₆H₁₇N₄O₃⁷⁹Br³⁵ClP: 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 Et₂O gave pure **20g** as a yellow solid; yield: 190 mg (48 %), mp 145 °C. UV/VIS (CH₂Cl₂): λ (log ε) = 234 (4.31), 306 (3.89), 356 (3.81). IR (KBr): ν [cm⁻¹] = 3271s/3141s (N-H), 2984s, 1629s, 1565s, 1463s, 1388s, 1341m, 1216s (P=O), 1172s, 1142m, 1101s, 1004s (P-O-C), 887m, 860m, 780m, 756m, 702m, 621m, 571s, 511m, 440m. ¹H-NMR (250.13 MHz, CDCl₃): δ [ppm]= 8.65 (1H, N-H), 6.62 (1H, N-H), 4.85-4.74 (m, 2H, P-O-CH₂-CH₃), 2.52 (s, 3H, CH₃ at C-7), 1.36 (d, 6H, ³J_{HH} = 6.1 Hz, P-O-CH(CH₃)₂), 1.29 (d, 6H, ³J_{HH} = 6.1 Hz, P-O-CH-

(CH₃)₂). ¹³C-NMR (90.56 MHz, CDCl₃): 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-CH-(H₃)₂), 23.97-23.74 (m, P-O-CH-(CH₃)₂), 13.13 (s, CH₃ at C-7). EI-MS : m/z (%) = 393 (24, [⁸¹Br-M]⁺), 391 (24, [⁷⁹Br-M]⁺), 335 (22, [⁸¹Br-M-C₃H₆O]⁺), 333 (22, [⁷⁹Br-M-C₃H₆O]⁺), 309 (100, [⁸¹Br-M-2C₃H₆]⁺), 307 (94, [⁷⁹Br-M-2C₃H₆O]⁺), 293 (18, [⁸¹Br-M-C₃H₆-C₃H₆O]⁺), 292 (22), 291 (32, [⁷⁹Br-M-C₃H₆-C₃H₆O]⁺), 290 (22), 289 (17), 229 (19, [⁸¹Br-M-PO(O-*i*-C₃H₇)₂+H]⁺), 227 (20, [⁷⁹Br-M-PO(O-*i*-C₃H₇)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 C₁₂H₁₉N₅O₃⁷⁹BrP: 391.0407. Found: 391.0405. Anal. Calcd for C₁₂H₁₉N₅O₃⁷⁹BrP: 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 CHCl₃ (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 (MgSO₄), 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 CHCl₃ (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 Et₂O for 24 h gave pure **20b** as a light brown solid; yield: 180 mg (43%), mp 142 °C. UV/VIS (CH₂Cl₂): λ (log ε)= 238 (4.29), 308 (3.93), 358 (3.88). IR: ν = 3376m/3270s (N-H), 2977m, 1606s, 1534s, 1384m, 1220s (P=O), 1167m, 1078m, 1023s (P-O-C), 983m, 776m, 565m, 494m. ¹H-NMR (250.13 MHz, CDCl₃): δ = 8.55 (1H, N-H), 6.50 (1H, N-H), 4.33-4.17 (m, 4H, P-O-CH₂-CH₃), 2.55 (s, 3H, CH₃ at C-7), 1.39-1.33 (m, 6H, P-O-CH₂-CH₃). ¹³C-NMR (62.89 MHz, DMSO-d₆): 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-CH₂-CH₃), 54.88 (s, C-8), 15.96 (d, ³J_{CP} = 5.8 Hz, P-O-CH₂-CH₃), 14.45 (s, CH₃ at C-7). EI-MS : m/z (%) = 412 (15, [M+1]⁺), 411 (100, [M]⁺), 367 (40, [M-C₂H₄O]⁺), 338 (50), 303 (73), 302 (34), 275 (91, [M-

PO(OC₂H₅)₂+HJ⁺), 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 C₁₀H₁₅N₅O₃IP: 410.9956. Found: 410.9957. Anal. Calcd for C₁₀H₁₅N₅O₃IP: 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 Et₂O 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 (CH₂Cl₂): λ (log ε) = 244 (4.71), 282 (3.78), 374 (3.56). IR (KBr): ν [cm⁻¹] = 3447m, 2986m, 1558m, 1472m, 1286m, 1245m, 1217m, 1057s, 1025s, 982m, 952m, 776m, 750m, 693m, 585m. ¹H-NMR (250.13 MHz, CDCl₃): 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-CH₂-CH₃), 2.55 (s, 3H, CH₃ at C-7), 1.21 (t, 6H, ³J_{HH} = 7.1 Hz, P-O-CH₂-CH₃). ¹³C-NMR (62.89 MHz, CDCl₃): 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-CH₂-CH₃), 56.79 (s, C-8), 16.11 (d, ³J_{CP} = 7.2 Hz, P-O-CH₂-CH₃), 15.19 (s, CH₃ at C-7). EI-MS : m/z (%) = 473 (19, [M+1]⁺), 472 (100, [M]⁺), 428 (40, [M-C₂H₄O]⁺), 427 (21), 399 (39), 364 (47), 363 (61), 336 (16), 335 (35, [M-PO(OC₂H₅)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 C₁₆H₁₈N₄O₃IP: 472.0160. Found: 472.0161. Anal. Calcd for C₁₆H₁₈N₄O₃IP: 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 Et₂O gave pure **20f** as an orange solid; yield: 80 mg (30 %), mp 151 °C. UV/VIS (CH₂Cl₂): λ (log ε) = 230 (4.16), 256 (4.51), 302sh (3.86), 396 (3.54). IR (KBr): ν [cm⁻¹] = 3123m/3101m/2901m (arom. H), 1603m, 1555s, 1521s, 1472s, 1443m, 1394m, 1348s, 1308m, 1247s/1221s (P=O), 1161m, 1104m, 1057s/1026s (P-O-C), 977s, 948s, 917m, 849s, 811m, 772m, 752m, 693m, 586s, 534m, 466m. ¹H-NMR (250.13 MHz, CDCl₃): 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-CH₂-CH₃), 2.56 (s, 3H, CH₃ at C-7), 1.27 (t, 6H, ³J_{HH} = 6.9 Hz, P-O-CH₂-CH₃). ¹³C-NMR (62.89 MHz, CDCl₃): 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-CH₂-CH₃), 57.77 (s, C-8), 16.20 (d, ³J_{CP} = 6.6 Hz, P-O-CH₂-CH₃), 15.14 (s, CH₃ at C-7). EI-MS : m/z (%) = 518 (19, [M+1]⁺), 517 (100, [M]⁺), 473 (35, [M-C₂H₄O]⁺), 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 C₁₆H₁₇N₅O₅IP: 517.0010. Found: 517.0010. Anal. Calcd for C₁₆H₁₇N₅O₅IP: 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 Et₂O for 2 h gave pure **20h** as a brown solid; yield: 655 mg (74 %), mp 125-127 °C. UV/VIS (CH₂Cl₂): λ (log ε) = 238 (4.24), 306 (3.87), 358 (3.84). IR (KBr): ν [cm⁻¹] = 3268s/3137s (N-H), 2980m, 1700m, 1627s, 1559s, 1451m, 1386m, 1339m, 1217s (P=O), 1166m, 1100m, 1002s (P-O-C), 887w, 851m, 779m, 756m, 701w, 620w, 566m, 509m, 429w. ¹H-NMR (250.13 MHz, CDCl₃): δ [ppm]= 8.61 (1H, N-H), 6.51 (1H, N-H), 4.83-4.70 (m, 2H, P-O-CH-(CH₃)₂), 2.52 (s, 3H, CH₃ at C-7), 1.34 (d, 6H, ³J_{HH} = 6.1 Hz, P-O-CH-(CH₃)₂), 1.29 (d, 6H, ³J_{HH} = 6.1 Hz, P-O-CH-(CH₃)₂). ¹³C-NMR (62.89 MHz, CDCl₃): 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-CH-(CH₃)₂), 23.99-23.75 (m, P-O-CH-(CH₃)₂), 14.85 (s, CH₃ at C-7). EI-MS : m/z (%) = 440 (7, [M+1]⁺), 439 (45, [M+1]⁺), 381 (27), 356 (10), 355 (100, [M-2 C₃H₆]⁺), 339 (17, [M-C₃H₆O-C₃H₆]⁺), 338 (24), 337 (18), 275 (22, [M-PO(O-*i*-C₃H₇)₂+H]⁺), 223 (12), 82 (10), 66 (12), 65 (11), 43 (33), 41 (16). HR-MS: m/z Calcd for C₁₂H₁₉N₅O₃IP: 439.0269. Found: 439.270. Anal. calcd for C₁₂H₁₉N₅O₃IP: C, 32.82; H, 4.36; N, 15.95. Found: C, 33.03; H, 4.55; N, 15.95.

4-Amino-7-methyl-8-phenylethynylpyrazolo[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*-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 Et₂O for 3 h and in *n*-hexane for 24 h as a yellow solid. yield: 80 mg (20%), mp 75 °C. UV/VIS (CH₂Cl₂): λ (log ε) = 230 (4.32), 264sh (4.03), 328sh (3.39). IR: ν = 3051m, 1479m, 1433s, 1261m, 1093m, 1027m, 823m, 741s, 693s, 517s. ¹H-NMR (250.13 MHz, CDCl₃): 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-CH₂-CH₃), 2.61 (s, 3H, CH₃ at C-7), 1.36 (t, 6H, ³J_{HH} = 7.1 Hz, P-O-CH₂-CH₃). ¹³C-NMR (90.56 MHz, CDCl₃): 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-CH₂-CH₃), 15.90 (d, ³J_{CP} = 6.6 Hz, P-O-CH₂-CH₃), 13.13 (s, CH₃ 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 C₁₈H₂₀N₅O₃P: 385.1302. Found: 385.1300. Anal. Calcd for C₁₈H₂₀N₅O₃P: C, 56.10; H, 5.23; N, 18.17. Found: C, 56.33; H, 5.16; N, 18.30.

7-Methyl-4-phenyl-8-phenylethynylpyrazolo[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*-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 Et₂O 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 (CH₂Cl₂): λ (log ε) = 230 (4.30), 252sh (4.37), 262 (4.36), 288 (4.40), 330 (4.02), 420 (3.62). IR (KBr): ν [cm⁻¹] = 3446m, 3163m, 3061m, 2987m, 1773m, 1700m, 1635m, 1500m, 1479m, 1259s (P=O), 1184m,

1053s/1028s (P-O-C), 768m, 698m, 525m. $^1\text{H-NMR}$ (250.13 MHz, CDCl_3): δ [ppm]= 7.81-7.36 (m, 10 H, arom. H), 4.26-4.07 (m, 4H, P-O-CH₂-CH₃), 2.65 (s, 3H, CH₃ at C-7), 1.24-1.18 (m, 6H, P-O-CH₂-CH₃). $^{13}\text{C-NMR}$ (62.89 MHz, CDCl_3): δ [ppm]= 160.21 (s, C-7), 149.78 (s, C-8a), 139.57 (d, $^2J_{\text{CP}} = 29.1$ 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, $^1J_{\text{CP}} = 235.8$ Hz, C-3), 97.27 (s, sp-C), 97.11 (s, sp-C), 71.74 (s, C-8), 63.76 (d, $^2J_{\text{CP}} = 6.2$ Hz, P-O-CH₂-CH₃), 16.11 (d, $^3J_{\text{CP}} = 6.7$ Hz, P-O-CH₂-CH₃), 13.73 (s, CH₃ at C-7). EI-MS: m/z (%) = 447 (25, $[\text{M}+1]^+$), 446 (89, $[\text{M}]^+$), 373 (11, $[\text{M}-\text{C}_2\text{H}_5\text{O}-\text{C}_2\text{H}_4]^+$), 338 (14), 337 (24), 310 (35), 309 (56, $[\text{M}-\text{PO}(\text{OC}_2\text{H}_5)_2]^+$), 165 (10), 140 (23), 139 (100), 102 (17), 81 (13), 77 (11). HR-MS: m/z Calcd for $\text{C}_{24}\text{H}_{23}\text{N}_4\text{O}_3\text{P}$: 446.1508. Found: 446.1508. Anal. Calcd for $\text{C}_{24}\text{H}_{23}\text{N}_4\text{O}_3\text{P}$: C, 64.57; H, 5.19; N, 12.55. Found: C, 64.55; H, 5.23; N, 12.71.

4-Amino-7-methyl-8-phenylethynylpyrazolo[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)₂NH (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 Et₂O 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}] = 3271s/3139s (N-H), 2983m, 1628s, 1560s, 1463m, 1387m, 1343m, 1217s (P=O), 1172m, 1101m, 1004s (P-O-C), 860m, 780m, 743m, 701w, 621w, 571m, 511m. $^1\text{H-NMR}$ (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-CH-(CH₃)₂), 2.62 (s, 3H, CH₃ at C-7), 1.38 (d, 6H, $^3J_{\text{HH}} = 6.1$ Hz, P-O-CH-(CH₃)₂), 1.32 (d, 6H, $^3J_{\text{HH}} = 6.1$ Hz, P-O-CH-(CH₃)₂). $^{13}\text{C-NMR}$ (62.89 MHz, CDCl_3): δ [ppm]= 158.78 (s, C-7), 148.47 (s, C-8a), 142.47 (d, $^2J_{\text{CP}} = 30.9$ 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, $^1J_{\text{CP}} = 235.0$ Hz, C-3), 96.20 (s, sp-C), 95.33 (s, sp-C), 78.27 (s, C-8), 73.20 (d, $^2J_{\text{CP}} = 6.2$ Hz, P-O-CH-(CH₃)₂), 24.00-23.73 (m, P-O-CH-(CH₃)₂), 13.44 (s, CH₃ 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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