SYNTHESSES 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
Previously 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, pyrazolo[3,2-c][1,2,4]triazines and [1,2,4]triazolo[3,2-c][1,2,4]triazines are known. As analogues of the purine bases they may have a wide range of biological activity. 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 or Egge 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 CH₂Cl₂. 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

![Scheme 1](image)

Table 1

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Table 4

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Table 5

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Table 6

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Scheme 3

Table 7

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Table 8

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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 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-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 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, 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 dublett. $^{31}$P-NMR spectra proved the phosphonato moiety by single peaks with chemical shifts regularly between 8 and 13 ppm. Further NMR-studies showed the molecular structures as 4-amino or 4-hydroxy derivatives respectively, i.e. as bi-/tricyclic 10-/14-$\pi$ 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 %. 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](image)

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<td>I</td>
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</table>
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)\(^\text{11}\) (Scheme 8).

![Scheme 8](image)

### Table 10

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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; Et₂O and THF were distilled from Na/benzophenone, CH₂Cl₂ and CHCl₃ from CaH₂. 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 CH₂Cl₂ 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. ¹H-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. ¹³C-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 derivates (2) and (3) as well as the aroylmethylphosphonic acid diethyl esters (4) are described in literature. The diazobetaines were synthesized according to the literature 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 CH₂Cl₂ (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 CH₂Cl₂ (3x50 mL). The combined organic layers were dried (MgSO₄) 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$_2$Cl$_2$ (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$_2$O gave pure 5a as a yellow solid; yield: 620 mg (22%), mp 184-185 °C. UV/VIS (CH$_2$Cl$_2$): $\lambda$ (log $\varepsilon$) = 228 (4.17), 256 (4.34), 368 (4.11), 386$sh$ (4.04). IR: $\nu$ = 3338s/3157s (N-H), 2957m, 2853m, 1613m, 1560m, 1528m, 1440s, 1365s, 1250s, 11229s (P=O), 1060s/1037s (P=O-C), 970m, 833s, 780s, 754s, 738m, 668m, 627m, 551s, 474s. $^1$H-NMR (299.95 MHz, DMSO-d$_6$): $\delta$ = 9.18 (s, 1H, N-H), 8.42 (d, $^3$J$_{HH}$ = 8.3 Hz, 1H, arom.H), 8.38 (s, 1H, N-H), 7.94 (d, $^3$J$_{HH}$ = 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-CH$_3$), 3.81 (s, 3H, P=O-CH$_3$). $^{13}$C-NMR (75.43 MHz, DMSO-d$_6$): $\delta$ = 149.91 (s, C-6a), 142.96 (d, $^2$J$_{CP}$ = 31.6 Hz, C-4), 130.94 (s, C-8), 122.36 (s, C-10), 120.73 (s, C-9), 118.47 (d, $^1$J$_{CP}$ = 232.0 Hz, C-3), 112.62 (s, C-10a), 53.70 (d, $^2$J$_{CP}$ = 5.2 Hz, P=O-CH$_3$). $^{31}$P-NMR (121.42 MHz, DMSO-d$_6$): $\delta$ = 13.79 (s). El-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$_5$O$_3$P: 293.0677, found: 293.0676. Anal. Calcd for C$_{11}$H$_{12}$N$_5$O$_3$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 (Et$_2$O/CH$_2$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$_2$Cl$_2$): $\lambda$ (log $\varepsilon$) = 228 (4.15), 256 (4.35), 368 (4.14), 380 (4.10). IR (KBr): $\nu$ [cm$^{-1}$] = 3353m (NH), 3158m, 2983m, 2344w, 1612s, 1527m, 1357m, 1247s (P=O), 1023s (P=O-C), 971s, 698s. $^1$H-NMR (299.95 MHz, CDCl$_3$): $\delta$ [ppm] = 8.69 (1H, N-H), 8.44 (d, $^1$H, $^3$J$_{HH}$ = 8.4 Hz, H-7), 7.80 (d, 1H, $^3$J$_{HH}$ = 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, J_HH = 7.1 Hz, C-O-CH₂-CH₃). ¹³C-NMR (75.43 MHz, CDCl₃): δ [ppm] = 150.7 (s, C-6a), 143.5 (d, J_CP = 2.1 Hz, C-10b), 142.3 (d, J_CP = 30.9 Hz, C-4), 131.1 (s, C-8), 122.8 (s, C-10), 121.2 (s, C-9), 119.9 (d, J_CP = 232.8 Hz, C-3), 116.1 (s, C-7), 113.6 (s, C-10a), 64.2 (d, J_CP = 6.0 Hz, C-O-CH₂-CH₃), 16.2 (d, J_CP = 6.6 Hz, C-O-CH₂-CH₃).

I3c~MR (75.43 MHz, CDCl₃): δ [ppm] = 150.7 (s, C-6a), 143.5 (d, J_CP = 2.1 Hz, C-10b), 142.3 (d, J_CP = 30.9 Hz, C-4), 131.1 (s, C-8), 122.8 (s, C-10), 121.2 (s, C-9), 119.9 (d, J_CP = 232.8 Hz, C-3), 116.1 (s, C-7), 113.6 (s, C-10a), 64.2 (d, J_CP = 6.0 Hz, C-O-CH₂-CH₃), 16.2 (d, J_CP = 6.6 Hz, C-O-CH₂-CH₃).

IR (KBr): ν [cm⁻¹] = 3340m/3161m/2984m (N-H), 1616s, 1548m, 1441m, 1388m, 1374m, 1357m, 1247s/11229s (P=O), 1177m, 1104m, 1066s (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, J_HH = 6.1 Hz, P-O-CH-(CH₃)₂), 1.34 (d, J_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, J_CP = 2.0 Hz, C-10b), 142.00 (d, J_CP = 31.0 Hz, C-4), 131.25 (s, C-8), 122.58 (s, C-10), 121.26 (s, C-9), 120.89 (d, J_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). El-MS: m/z (%) = 350 (7, [M+1]⁺), 349 (38, [M]⁺), 307 (10, [M-C₃H₆]⁺), 266 (13), 265 (100, [M-2C₃H₇O]⁺), 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, 51.34; H, 5.77; N, 20.19. Found: C, 51.34; H, 5.88; N, 20.19.

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, 1066s (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, J_HH = 6.1 Hz, P-O-CH-(CH₃)₂), 1.34 (d, J_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, J_CP = 2.0 Hz, C-10b), 142.00 (d, J_CP = 31.0 Hz, C-4), 131.25 (s, C-8), 122.58 (s, C-10), 121.26 (s, C-9), 120.89 (d, J_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). El-MS: m/z (%) = 350 (7, [M+1]⁺), 349 (38, [M]⁺), 307 (10, [M-C₃H₆]⁺), 266 (13), 265 (100, [M-2C₃H₇O]⁺), 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, 51.34; 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), 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-0-C), 752 s, 568 s.

¹H-NMR (299.95 MHz, CDCl₃): δ [ppm] = 8.42 (d, 3JHH = 8.6 Hz, 1H, arom. H), 7.84 (d, 3JHH = 8.9 Hz, 1H, arom. H), 7.58 (m, 1H, arom. H), 7.28 (t, 3JHH = 7.6 Hz, 1H, arom. H), 4.53-4.37 (m, 4H, P-0-CH₂-CH₃), 1.46 (t, 3JHH = 7.0 Hz, 6H, P-0-CH₂-CH₃).

¹³C-NMR (75.43 MHz, CDCl₃): δ [ppm] = 149.86 (s, C-6a), 148.96 (d, 2JCp = 25.2 Hz, C-4), 136.94 (s, C-lob), 131.25 (s, C-8), 123.04 (s, C-3), 121.03 (s, C-9), 117.45 (s, C-7), 107.72 (s, C-10a), 64.54 (d, 2JCp = 6.0 Hz, P-O-CH₂-CH₃), 16.36 (d, 3JCp = 6.5 Hz, P-O-CH₂-CH₃).


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] = 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. ¹H-NMR (250.13 MHz, CDCl₃): δ [ppm] = 8.50 (d, 1H, 3JHH = 8.5 Hz, arom. H), 7.88 (d, 1H, 3JHH = 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, 3JHH = 6.2 Hz, P-O-CH-(CH₃)₂), 1.41 (d, 6H, 3JHH = 6.2 Hz, P-O-CH-(CH₃)₂). ¹³C-NMR (90.56 MHz, CDCl₃): δ [ppm] = 150.28 (s, C-6a), 149.01 (d, 2JCp = 25.3 Hz, C-4), 137.40 (s, C-10b), 131.33 (s, C-8), 128.52 (d, 1JCp = 233.46 Hz, C-3), 123.11 (s, C-10), 121.30 (s, C-9), 117.45 (s, C-7), 107.72 (s, C-10a), 64.54 (d, 2JCp = 6.0 Hz, P-O-CH₂-CH₃), 16.36 (d, 3JCp = 6.5 Hz, P-O-CH₂-CH₃).
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): \( \lambda \) (log \( \varepsilon \)) = 230 (4.21), 294 (3.90), 352 (4.07). IR: \( \nu \) = 3365s (N-H), 3275m, 3227m, 2984m, 1685s (GO), 1629%, 1565s, 1497s, 1440m, 1288m, 1226s (P=O), 1141m, 1027s (P-0-C), 971m, 782s, 576s, 517s. \(^{1}H\)-NMR (250.13 MHz, CDCl3): \( \delta \) = 8.71 (s, 1H, N-H), 8.62 (s, IH, H-7), 6.85 (s, IH, N-H), 4.50 (q, 2H, \( ^{3}J_{HH} = 7.1 \) Hz, C-O-CH2-CH3), 4.37-4.20 (m, 4H, P-0-CH2-CH3), 4.16 (t, 3H, \( ^{3}J_{HH} = 7.1 \) Hz, C-O-CH2-CH3). \( ^{31}P\)-NMR (121.42 MHz, CDCl3): \( \delta \) = 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, \([M-2C_{3}H_{7}]^{+}\)), 238 (39, \([M-2C_{3}H_{7}-N_{2}]^{+}\)), 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_{4}O_{4}P: 350.1145. Found: 350.1146. Anal. Calcd for C_{15}H_{19}N_{4}O_{4}P: C, 51.54; H, 5.44; N, 15.76.

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$_2$O), followed by treatment with n-hexane in boiling Et$_2$O and recrystallisation from Et$_2$O, gave pure 9b as a white, crystalline solid; yield: 490 mg (13%), mp 124 °C. UV/VIS (CH$_2$Cl$_2$): $\lambda$ (log $\varepsilon$) = 230 (4.35), 296 (4.00), 352 (4.18). IR (KBr): $\nu$ [cm$^{-1}$] = 3366m (N-H), 3275m, 3224m, 2983m, 1692s (C=O), 1628s, 1566m, 1497m, 1437m, 1386m, 1202m, 1185s (P=O). UVNMR (299.95 MHz, CDCl$_3$): $\delta$ [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$_2$-CH$_3$), 4.50 (s, 2H, P-O-CH$_2$-CH$_3$), 1.38 (d, 6H, J$_{HP}$ = 6.3 Hz, P-O-CH$_2$-CH$_3$). IR (KBr): $\nu$ [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. UVNMR (299.95 MHz, CDCl$_3$): $\delta$ [ppm] = 161.70 (s, C=O), 148.16 (s, C-7), 146.52 (d, J$_{CP}$ = 2.0 Hz, C-8a), 142.57 (d, J$_{CP}$ = 31.3 Hz, C-4), 120.97 (d, J$_{CP}$ = 234.8 Hz, C-3), 104.57 (s, C-8), 73.49 (d, J$_{CP}$ = 6.3 Hz, C-O-CH$_2$-CH$_3$), 23.94-23.74 (m, C-O-CH$_2$-CH$_3$), 14.50 (s, C-O-CH$_2$-CH$_3$). 31P-NMR (121.42 MHz, CDCl$_3$): $\delta$ [ppm] = 8.01 (s). HR-MS m/z Calcd for C$_{14}$H$_{22}$N$_5$O$_5$P: 371.1357. Found: 371.1355. Anal. Calcd for C$_{14}$H$_{22}$N$_5$O$_5$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$_2$Cl$_2$ solution of 9c with Et$_2$O caused precipitation of crude 9c. This was purified by recrystallisation from Et$_2$O as a brown solid; yield: 1.86 g (41%), mp 126 °C. UV/VIS (CH$_2$Cl$_2$): $\lambda$ (log $\varepsilon$) = 232 (4.42), 298 (3.88), 344 (3.80). IR: $\nu$ = 3336m / 3141s (N-H), 2983m, 1628s, 1572s, 1390m, 1272m, 1245m, 1213s (P=O), 1080m, 1040s (P-O-C), 973m, 959m, 799m, 751m, 657m, 579m, 518m. 1H-NMR (299.95 MHz, CDCl$_3$): $\delta$ = 8.43 (s, 1H, N-H), 6.78 (s, 1H, H-8), 6.63 (s, 1H, H-8), 4.37-4.15 (m, 4H, P-O-CH$_2$-CH$_3$), 2.56 (s, 3H, CH$_3$ at C-7), 1.37 (dt, 6H, J$_{HP}$ = 7.1 Hz, J$_{CP}$ = 0.7 Hz, P-O-CH$_2$-CH$_3$). 13C-NMR (75.43 MHz, CDCl$_3$): $\delta$ = 156.54 (C-7), 149.39 (d, J$_{CP}$ = 2.0 Hz, C-8a), 142.57 (d, J$_{CP}$ = 31.0 Hz, C-4), 115.66 (d, J$_{CP}$ = 236.9 Hz, C-3),
97.97 (s, C-8), 63.73 (d, J_C_P = 5.9 Hz, P-O-\text{CH}_2-\text{CH}_3), 16.20 (d, J_C_P = 6.8 Hz, P-O-\text{CH}_2-\text{CH}_3), 14.54 (s, \text{CH}_3 \text{ at C-7}). ^{31}P-NMR (121.42 MHz, CDCl₃): δ = 12.65 (s). El-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. lH-NMR (250.13 MHz, CDCl₃): δ [ppm] = 8.28 (s, H-7), 4.44-4.32 (m, 6H, C-₀-CH₂-CH₃, P-₀-CH₂-CH₃), 1.42-1.37 (m, 9H, C-₀-CH₂-CH₃, P-₀-CH₂-CH₃). ¹³C-NMR (62.89 MHz, CDCl₃): δ [ppm] = 161.71 (s, GO), 147.78 (d, J_C_P = 24.6 Hz, C-4), 144.91 (s, C-7), 143.44 (s, C-8a), 134.91 (d, J_C_P = 234.8 Hz, C-3), 98.60 (s, C-8), 64.51 (d, J_C_P = 6.2 Hz, P-O-CH₂-CH₃), 61.36 (s, C-₀-CH₂-CH₃), 16.40 (d, J_C_P = 6.2 Hz, P-O-CH₂-CH₃), 14.41 (s, C-₀-CH₂-CH₃).


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 =
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 (CH2Cl2): λ (log ε) = 230sh (3.82), 254 (4.42), 318 (3.83). IR (KBr): ν [cm⁻¹] = 3080s, 2908s, 2750s, 2729s, 1523m, 1450s, 1388s (P=O), 1102w, 1030s (P-O-C), 999s, 857w, 709s, 581w. ¹H-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, JHH = 6.2 Hz, P-O-CH(CH3)2), 1.28 (d, 6H, JHH = 6.1 Hz, P-O-CH(CH3)2). ¹³C-NMR (62.89 MHz, acetone-d6): δ [ppm]= 170.67 (s, C-7), 157.01 (s, C-8a), 144.20 (d, JCP = 33.8 Hz, C-4), 123.73 (d, JCP = 234.3 Hz, C-3), 73.32 (d, JCP = 5.2 Hz, P-O-CH(CH3)2), 24.14-23.87 (m, P-O-CH(CH3)2), 13.90 (s, S-CH3). ³¹P-NMR (121.42 MHz, acetone-d6): δ [ppm]= 7.23 (s). EI-MS: m/z (%) = 347 (5, [M+1]^+) 346 (33, [M]^+), 289 (19), 288 (73, [M-C3H6O]^+), 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 C₁₁H₁₉N₆O₃PS: 346.0977. Found: 346.0977.

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_{2}Cl_{2}): λ (log ε) = 236 (4.29), 312 (3.82). IR (KBr): ν [cm^{-1}] = 3420m (O-H), 3211w, 3126w, 2982s / 2930s (S-CH_{3}), 2772s, 1724s, 1510s, 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-CH_{2}-CH_{3}), 2.69 (s, 3H, S-CH_{3}), 1.40 (dt, 6H, J_{HH} = 7.1 Hz, J_{HP} = 0.7 Hz, P-O-CH_{2}-CH_{3}). 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-CH_{2}-CH_{3}), 16.28 (d, 3J_{CP} = 6.5 Hz, P-O-CH_{2}-CH_{3}), 14.05 (s, S-CH_{3}). 31P-NMR (121.42 MHz, CDCl_{3}): δ [ppm]= 6.60 (s). El-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_{9}H_{14}N_{5}O_{4}PS: 319.0503. Found: 319.0502. Anal. Calcd for C_{9}H_{14}N_{5}O_{4}PS: 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_{2}Cl_{2}): λ (log ε) = 238 (4.31), 310 (3.87). IR (KBr): ν [cm^{-1}] = 3420m (O-H), 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-d_{6} ): δ [ppm] = 4.73 (q, 2H, J_{HH} = 6.4 Hz, P-O-CH-(CH_{3})_{2}), 2.67 (s, 3H, S-CH_{3}), 1.18 (m, 12H, P-O-CH-.
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(CH$_3$)$_2$. $^{13}$C-NMR (75.43 MHz, acetone-$d_6$): $\delta$ [ppm] = 167.67 (s, C-7), 157.85 (s, C-8a), 151.06 (d, $^2$J$_{CP}$ = 29.6 Hz, C-4), 131.39 (d, $^1$J$_{CP}$ = 235.1 Hz, C-3), 73.03 (d, $^2$J$_{CP}$ = 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$_3$).

El-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$_5$O$_4$PS: 347.0817. Found: 347.0817. Anal. Calcd for C$_{11}$H$_{18}$N$_5$O$_4$PS: 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-arylpurazolo[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$_2$O gave pure 7a as an orange solid; yield: 85 mg (2 %), mp 146-147 °C. UV/VIS (CH$_2$Cl$_2$): $\lambda$ (log $\varepsilon$) = 230 (4.28), 242 (4.18), 282 (4.47), 352 (3.74), 366 (3.75), 422 (3.43). IR (KBr): v [cm$^{-1}$] = 3448m, 3057w, 2979w, 1631m, 1507w, 1468m, 1445m, 1350m, 1295m, 1262s (P=O), 1202m, 1170m, 1054m, 1025s (P-O-C), 979m, 771m, 697m, 645m, 580m, 546m, 508m. $^1$H-NMR (299.95 MHz, CDCl$_3$): $\delta$ [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, $^3$J$_{HH}$ = 6.9 Hz, P-O-CH$_2$-CH$_3$).

$^{13}$C-NMR (90.56 MHz, CDCl$_3$): $\delta$ [ppm] = 151.71 (s, C-6a), 145.97 (s, C-10b), 139.46 (d, $^1$J$_{CP}$ = 233.4 Hz, C-3), 137.26 (d, $^2$J$_{CP}$ = 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, $^2$J$_{CP}$ = 6.4 Hz, P-O-CH$_2$-CH$_3$), 16.17 (d, $^3$J$_{CP}$ = 6.9 Hz, P-O-CH$_2$-CH$_3$). El-MS: m/z (%) = 383 (24, [M+1]+), 382 (100, [M]+), 367 (17),

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 Et2O 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 CHCl3; yield: 408 mg (98%), mp 146-147 °C. UV/VIS (CH2Cl2): 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 m, 1261 s (P=O), 1200 m, 1171 m, 1092 m, 1031 s (P-O-C), 983 s, 955 m, 834 m, 763%, 544 m, 518 m. 1H-NMR (250.13 MHz, CDCl3): 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-CH2-CH3), 1.31-1.26 (m, 6H, P-O-CH2-CH3). 13C-NMR (62.89 MHz, CDCl3): δ = 151.73 (s, C-6a), 145.98 (d, JCP = 3.1 Hz, C-10b), 139.40 (d, JCP = 233.1 Hz, C-3), 137.86 (s, C-4'), 136.74 (d, JCP = 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, JCP = 6.9 Hz, P-O-CH2-CH3), 16.20 (d, JCP = 7.0 Hz, P-O-CH2-CH3). 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 C19H18N4O3ClP: 416.0803. Found: 416.0801. Anal. Calcd for C19H18N4O3ClP: 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-ylicarbonic 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 Et2O 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 CHCl₃; yield: 390 mg (96 %), mp 104 °C. UV/VIS (CH₂Cl₂): λ (log ε) = 232sh (4.17), 248 (4.30), 296 (3.73), 308sh (3.70), 356 (3.61), 390sh (3.52). IR: v = 3431m, 2979m, 1726s (C=O), 1576s, 1476s, 1340s, 1273s, 1201s (P=O), 1142s, 1051s/1019s (P-O-C), 982m, 751m, 702m, 531s. ¹H-NMR (299.95 MHz, CDCl₃): δ = 8.72 (s, 1H, H-7), 7.81-7.63 (m, 5H, arom. H), 4.55 (q, 2H, ³JHH = 7.1 Hz, C-O-CH₂-CH₃), 1.48 (t, 3H, ³JHH = 7.1 Hz, P-0-CH₂-CH₃). ¹³C-NMR (90.56 MHz, CDCl₃): δ = 161.36 (s, C=O), 149.45 (s, C-7), 147.78 (s, C-8a), 140.03 (d, ²JCp = 28.9 Hz, C-4), 138.15 (d, ¹JCp = 235.0 Hz, C-3), 131.94 (s, C-4'), 128.57 (s, arom. C), 126.23 (s, C-3'), 114.10 (s, arom. C), 106.24 (s, C-8), 64.04 (d, ²JCp = 6.3 Hz, P-0-C₂H₂-CH₃), 61.38 (s, C-0-CH₂-CH₃), 16.14 (d, ³JCp = 6.7 Hz, P-O-CH₂-CH₃), 14.51 (s, C-0-CH₂-CH₃). ³¹P-NMR (121.42 MHz, CDCl₃): δ = 7.86 (s). El-MS: m/z (%): 406 (3), 405 (20, [M+1]⁺), 404 (100, [M]⁺), 375 (11, [M-C₂H₅]⁺), 360 (37), 359 (35, [M-C₂H₅O]⁺), 358 (29), 331 (33, [M-COOC₂H₅]⁺), 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 C₁₈H₂₁N₄O₅P: 404.1248. Found: 404.1246. Anal. Calcd for C₁₈H₂₁N₄O₅P: 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 Et₂O gave pure 11b as a yellow solid; yield: 210 mg (5 %), mp 130 °C. UV/VIS (CH₂Cl₂): λ (log ε) = 232sh (4.38), 248 (4.45), 298 (3.89), 358 (3.77), 378sh (3.75). IR (KBr): v [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. ¹H-NMR (250.13 MHz, CDCl₃): δ [ppm] = 8.71 (s, 1H, H-7), 7.70 (d, 2H, ³JHH = 8.0 Hz, C-H), 7.43 (d, 2H, ³JHH = 8.0 Hz, C-H), 4.54 (q, 2H, ³JHH = 7.1 Hz, C-O-CH₂-CH₃), 4.29-4.13 (m, 4H, P-O-CH₂-CH₃), 2.49 (s, 3H, C₆H₄-CH₃), 1.48 (t, 3H, ³JHH = 7.1 Hz, C-O-CH₂-CH₃), 1.24 (t, 6H, ³JHH = 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, CH₃).

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), 286 (3.74). IR (KBr): ν [cm⁻¹] = 3419s, 2986m, 1558m, 1514w, 1468s, 1444~. 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).
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 Et₂O gave pure 11d as a yellow solid; yield: 880 mg (21 %), mp 117 °C. UV/VIS (CH₂Cl₂): 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), 1217% 1174w, 1111m, 1048s, 11020s (P-OX), 975s, 948m, 827m, 785m, 723m, 585s, 533m, 497w. ¹H-NMR (299.95 MHz, CDCl₃): 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-0-CH₂-CH₃), 2.57 (s, 3H, CH₃), 1.26 (t, 6H, 3H 7.1 Hz, P-0-CH₂-CH₃). ¹³C-NMR (90.56 MHz, CDCl₃): δ [ppm] = 158.52 (s, C-7), 150.99 (d, J_CP = 2.1 Hz, C-8a), 138.20 (d, J_CP = 29.9 Hz, C-4), 137.74 (s, C-4'), 134.74 (d, J_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, J_CP = 6.3 Hz, P-O-CH₂-CH₃), 16.16 (d, J_CP = 6.4 Hz, P-O-CH₂-CH₃). ²⁸P-NMR (121.42 MHz, CDCl₃): 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-C₂H₄O]⁺), 335 (28, [M-C₂H₅O]⁺), 309 (17), 308 (12), 307 (47, [M-C₂H₄O-C₂H₄]⁺), 292 (11), 274 (15), 273 (32), 272 (45), 271 (64), 246 (27), 245 (25), 244 (75, [M-PO(OCC₂H₅)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 C₁₆H₁₈N₄O₃P: 380.0806. Found: 380.0807. Anal. Calcd for C₁₆H₁₈N₄O₃P: 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 (CH₂Cl₂): 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,
1058 s / 1025 s (P-O-C), 989 m, 962 m, 783 m, 711 m, 640 m, 568 m.  

$^1$H-NMR (250.13 MHz, CDCl$_3$): $\delta = 7.87-7.84$ (m, 2H, C-2', C-6'), 7.70-7.57 (m, 3H, arom. H), 4.28 (m, 4H, P-O-CH$_2$-CH$_3$), 2.73 (s, 3H, S-CH$_3$), 1.21 (t, 6H, $^3$J$_{HH} = 7.2$ Hz, P-O-CH$_2$-CH$_3$).  

$^{13}$C-NMR (75.43 MHz, CDCl$_3$): $\delta = 174.00$ (s, C-7), 156.28 (d, $^4$J$_{CP} = 2.6$ Hz, C-8a), 139.13 (d, $^2$J$_{CP} = 30.4$ Hz, C-4), 138.99 (d, $^1$J$_{CP} = 237.0$ 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, $^2$J$_{CP} = 6.5$ Hz, P-O-CH$_2$-CH$_3$).  

$^{31}$P-NMR (121.42 MHz, CDCl$_3$): $\delta = 7.76$ (s). El-MS: m/z (%) = 380 (12, [M+I]$^+$), 379 (74, [M]$^+$), 350 (15), 335 (33), 334 (18, [M-C$_2$H$_5$O]$^+$), 332 (13), 306 (31, [M-C$_2$H$_5$O-C$_2$H$_4$]$^+$), 271 (34), 270 (47), 260 (11), 242 (16), 229 (15), 228 (100), 224 (10), 144 (9), 129 (9), 115 (10), 144 (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$_5$O$_3$P$^-$: 379.0867. Found: 379.0867. Anal. Calcd for C$_{15}$H$_{18}$N$_5$O$_3$P$^-$: 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$_2$O gave pure 15b as light yellow needles; yield: 450 mg (11 %), mp 150-151 °C. UV/VIS (CH$_2$Cl$_2$): $\lambda$ (log $\varepsilon$) = 254 (4.18), 330 (3.06). IR (KBr): $\nu$ [cm$^{-1}$] = 2980 m/2903 m (C-H), 1734 s, 1685 s, 1604 s, 1444 w, 1419 w, 1366 w, 1253 s (P=O), 1166 m, 1145 m, 1021 s (P-O-C), 973 s, 835 m, 753 m, 607 m, 518 m, 473 m.  

$^1$H-NMR (299.95 MHz, CDCl$_3$): $\delta$ [ppm] = 7.78 (d, 2H, $^3$J$_{HH} = 8.1$ Hz, H-2', H-6'), 7.42 (d, 2H, $^3$J$_{HH} = 8.1$ Hz, H-3', H-5'), 4.28-4.11 (m, 4H, P-O-CH$_2$-CH$_3$), 2.74 (s, 3H, S-CH$_3$), 2.49 (s, 3H, arom. CH$_3$), 1.23 (t, $^3$J$_{HH} = 7.1$ Hz, P-O-CH$_2$-CH$_3$).  

$^{13}$C-NMR (62.89 MHz, CDCl$_3$): $\delta$ [ppm] = 156.56 (s, C-7), 143.03 (s, C-8a), 139.75 (d, $^2$J$_{CP} = 30.6$ Hz, C-4), 139.16 (d, $^1$J$_{CP} = 236.3$ 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, $^2$J$_{CP} = 6.2$ Hz, P-O-CH$_2$-CH$_3$), 21.79 (s, arom. CH$_3$), 16.09 (d, $^3$J$_{CP} = 7.0$ Hz, P-O-CH$_2$-CH$_3$), 14.11 (s, S-CH$_3$). $^{31}$P-NMR (121.42 MHz, CDCl$_3$): $\delta$ [ppm] = 7.71 (s). El-MS: m/z (%) = 395 (4), 394 (13, [M+I]$^+$), 393 (67, [M]$^+$), 364 (12), 349 (14), 346
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/NIR (CH2Cl2): \( \lambda \) (log \( E \)) = 228 (4.31), 282 (4.24), 368 (4.06). IR: \( \nu = 3289 \text{s (N-H)}, 2983 \text{m}, 1636 \text{s (C=O)}, 1590 \text{m}, 1559 \text{s}, 1517 \text{m}, 1437 \text{m}, 1398 \text{s}, 1387 \text{s}, 1294 \text{s}, 1262 \text{s (P=O)}, 1273 \text{m}, 1092 \text{m}, 1020 \text{s (P-O-C)}, 983 \text{s}, 869 \text{m}, 804 \text{m}, 762 \text{m}, 745 \text{m}, 589 \text{m}. \( ^1H \)-NMR (250.13 MHz, CDCl3): \( \delta = 13.48 \text{ (s, IH, N-H)}, 10.52 \text{ (s, IH, N-H)}, 7.98-6.84 \text{ (m, 8H, arom. H)}, 4.39-4.22 \text{ (m, 4H, P-O-CH2-CH3)}, 1.43-1.23 \text{ (m, 6H, P-O-CH2-CH3)}. \( ^{13}C \)-NMR (62.89 MHz, CDCl3): \( \delta = 191.07 \text{ (d, }\text{J}_{\text{CP}} = 21.7 \text{ Hz, C-2)}, 151.74 \text{ (s, C-4'), 145.26 \text{ (s, C-8')}, 141.87 \text{ (s, C-3'), 137.75 \text{ (s, C-1'')}, 131.80 \text{ (s, C-6'), 131.21 \text{ (s, C-2'', C-6'')}, 128.33 \text{ (s, C-3'', C-5''), 127.99 \text{ (d, }\text{J}_{\text{CP}} = 155.7 \text{ Hz, C-1)}, 121.87 \text{ (s, C-4'), 120.83 \text{ (s, C-5'), 113.09 \text{ (s, C-9')}, 109.94 \text{ (s, C-7')}, 64.17-63.96 \text{ (m, P-O-CH2-CH3)}, 16.38-16.14 \text{ (m, P-O-CH2-CH3)}. EI-MS: m/z (%) = 436 (12, [M+2]^+), 435 (8, [M+1]^+), 434 (31, [M]^+), 416 (16, [M-H2O]^+), 297 (9, [M-PO(OOC2H5)2]^+), 295 (31, [M-35Cl-C6H4-CO]^+), 280 (15), 253 (17), 243 (13), 239 (10), 141 (32, [37Cl-C6H4-CO]^+), 139 (100, [35Cl-C6H4-CO]^+), 132 (19), 116 (32), 111 (20, [35Cl-C6H4]^+), 108 (16), 102 (13), 77 (18). HR-MS: m/z Calcd for C16H20N5O3PS: 393.1026. Found: 393.1028. Anal. Calcd for C16H20N5O3PS: 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.

3-Diethylphosphonato-4-hydroxy-4-phenylpyrazolo[3,2-c][2H,5H][1,2,4]triazin-8-ylcarboxylic 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 (CH2Cl2): \( \lambda \) (log \( E \)) = 230 (4.08), 306 (4.12). IR: \( \nu = 3303 \text{s/3144s (NH,OH)}, 2982 \text{m}, 1666 \text{s (C=O)}, 1603 \text{s}, 1545 \text{s}, 1287 \text{m}, 1228 \text{s (P=O)}, 1162 \text{m}, 1127 \text{m},
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 CHCl₃ (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 (MgSO₄), 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 Et₂O gave pure 20a as a yellowish solid; yield: 230 mg (63 %), mp 149 °C. UV/Vis (CH₂Cl₂): λ (log ε) = 232 (4.41), 304 (3.96), 356 (3.88). IR: ν = 3269s (N-H), 2989m, 1625s, 1560%, 1465m, 1390m, 1218s (P=O), 1171m, 1080m, 1026s (P-O-C), 978m, 861m, 797m, 761s, 621m, 568s, 497s.

1H-NMR (250.13 MHz, CDCl₃): δ = 8.59 (1H, N-H), 6.98 (1H, N-H), 4.40-4.18 (m, 4H, P-0-CH₂-CH₃), 2.52 (s, 3H, CH₃), 1.37 (t, 6H, 3J_HH = 6.9 Hz, P-0-CH₂-CH₃). 13C-NMR (62.89 MHz, CDCl₃): 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-0-CH₂-H₃), 16.21 (d, 3J_CP = 6.2 Hz, P-O-CH₂-CH₃), 13.12 (s, CH₃ at C-7). EI-MS: m/z (%) = 366 (8), 365 (66), [⁸¹Br-
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): $\lambda$ (log $e$) = 230sh (4.08), 252 (4.52), 286 (3.69), 392 (3.44). IR (KBr): $\nu$ [cm$^{-1}$] = 3448m, 3162m, 3058m, 2926m, 2855m, 1772m, 1700s, 1515m, 1465m, 1375m, 1288m, 1251s (P=O), 1229m, 1178s, 1121w, 1050s, 1022s (P-O-C), 962m, 822m, 796m, 777m, 694m, 651m, 588m, 540m. $^1$H-NMR (250.13 MHz, CDCl$_3$): $\delta$ [ppm] = 7.78-7.74 (m, arom. H), 7.64-7.58 (m, 3H, arom. H), 4.24-4.07 (m, 4H, P=O-CH$_2$-CH$_3$), 2.54 (s, 3H, CH$_3$ at C-7), 1.21 (t, 6H, $^3$J$_{HH}$ = 7.1 Hz, P-O-CH$_2$-CH$_3$). $^{13}$C-NMR (90.56 MHz, CDCl$_3$): $\delta$ [ppm] = 156.96, 147.31 (d, $^4$J$_{CP}$ = 2.2 Hz, C-8a), 139.44 (d, $^2$J$_{CP}$ = 29.3 Hz, C-4), 135.94 (d, $^1$J$_{CP}$ = 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, $^2$J$_{CP}$ = 6.5 Hz, P-O-CH$_2$-CH$_3$), 16.09 (d, $^3$J$_{CP}$ = 7.2 Hz, P-O-CH$_2$-CH$_3$), 13.41 (s, CH$_3$ 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$_2$H$_4$O$]^+$), 381 (25), 380 (35, $[^{79}$Br-M-C$_2$H$_4$O$]^+$), 379 (19), 353 (33, $[^{81}$Br-M-C$_2$H$_4$O-C$_2$H$_5$]$^+$), 351 (38, $[^{79}$Br-M-C$_2$H$_4$O-C$_2$H$_5$]$^+$), 318 (32), 317 (59), 316 (36), 315 (52), 289 (37, $[^{81}$Br-M-PO(OCH$_2$H$_5$)$_2$]$^+$), 287 (31, $[^{79}$Br-M-PO(OCH$_2$H$_5$)$_2$]$^+$), 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$_4$O$_3$ $^{79}$BrP: 424.0299. Found: 424.0298. Anal. Calcd for C$_{16}$H$_{18}$N$_4$O$_3$ $^{79}$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 Et₂O for 12 h gave pure 20d as yellow needles; yield: 135 mg (93%), mp 120°C. UV/VIS (CH₂Cl₂): \( \lambda \) (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 (P-O-C), 978s, 837m, 801m, 773m, 688s, 547s, 509m. ¹H-NMR (250.13 MHz, CDCl₃): δ [ppm] = 7.73 (d, 2H, JHH = 8.5 Hz, H-3', H-5'), 7.58 (d, 2H, JHH = 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, JHH = 7.0 Hz, P-O-CH₂-CM₃). ¹³C-NMR (90.56 MHz, CDCl₃): δ [ppm] = 157.08 (s, C-7), 147.32 (s, C-8a), 138.39 (d, JCP = 29.2 Hz, C-4). 138.16 (s, C-4'), 135.91 (d, JCP = 237.0 Hz, C-3), 131.66 (s, C-2', C-6'), 128.89 (s, C-3', C-5'), 124.60 (s, C-1'), 117.11 (s, C-8), 63.92 (d, JCP = 6.9 Hz, P-O-CH₂-CH₃), 16.16 (d, JCP = 6.4 Hz, P-O-CH₂-CH₃). HR-MS: m/z Calcd for C₃₅H₂₇BrN₂₅O₇P: 457.9910. Found: 457.9910. Anal. Calcd for 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): \( \lambda \) (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, JHH = 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, ²JCP = 31.6 Hz, C-4), 118.20 (d, ¹JCP = 235.5 Hz, C-3), 86.70 (s, C-8), 73.17 (d, ²JCP = 6.3 Hz, P-O-CH-(CH₃)₂), 23.97-23.74 (m, P-O-CH-(CH₃)₂), 13.13 (s, CH₃ at C-7).

Iodo-7-methylpyrazolo[3,2-c][1,2,4]triazin-3-yl phosphoric 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-ido-7-methylpyrazolo[3,2-c][1,2,4]triazin-3-yl phosphonic 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, 13270s (N-H), 2977m, 1606s, 1534s, 1384m, 1220s (P=O), 1167m, 1078m, 1023s (P-0-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, ²JCP = 32.8 Hz, C-4), 116.86 (d, ¹JCP = 235.3 Hz, C-3), 63.00 (d, ²JCP = 5.9 Hz, P-O-CH₂-CH₃), 54.88 (s, C-8), 42.77 (d, ³JCP = 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-
8-lodo-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-0-CH₂-CH₃), 2.55 (s, 3H, CH₃ at C-7), 1.21 (t, 6H, 3J_HH = 7.1 Hz, P-0-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). El-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(OCC₂H₅)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 C₁₀H₁₅N₅O₃P: 410.9956. Found: 410.9957. Anal. Calcd for C₁₀H₁₅N₅O₃P: C, 29.21; H, 3.68; N, 17.03. Found: C, 29.56; H, 3.56; N, 16.83.

8-lodo-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, JHH = 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, JCP = 18.3 Hz, C-4), 137.72 (s, C-4'), 135.37 (d, JCP = 221.4 Hz, C-3), 132.61 (s, C-2', C-6'), 123.55 (s, C-3', C-5'), 64.08 (d, JCP = 6.8 Hz, P-O-CH₂-CH₃), 57.77 (s, C-8), 16.20 (d, JCP = 6.6 Hz, P-O-CH₂-CH₃), 15.14 (s, CH₃ at C-7).


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 (NH), 2980m, 1700m, 1627s, 1599s, 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, JHH = 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, JCP = 30.8 Hz, C-4), 118.47 (d, JCP = 236.4 z, C-3), 73.22 (d, JCP = 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)+H]+), 223 (12), 82 (10), 66 (12), 55 (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-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-Pr₂)NH (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: v = 3051, 1715, 1479m, 1433s, 1261m, 1093m, 1027m, 823m, 693s, 517s. 'H-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-0-CH₂-CH₃), 2.61 (s, 3H, CH₃ at C-7), 1.36 (t, 6H, J_H-H = 7.1 Hz, P-0-CH₂-CH₃). ¹³C-NMR (90.56 MHz, CDCl₃): δ = 158.38 (s, C-7), 148.15 (s, C-8a), 142.50 (d, J 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, J CP = 236.7 Hz, C-3), 95.86 (s, sp-C), 94.92 (s, sp-C), 77.97 (s, C-7), 63.84 (d, J CP = 5.8 Hz, P-O-CH₂-CH₃), 15.90 (d, J CP = 6.6 Hz, P-O-CH₂-CH₃), 13.13 (s, CH₃ at C-7). El-MS: m/z (%) = 386 (21, [M+]⁺), 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-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-Pr₂)NH (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): v [cm⁻¹] = 3446m, 3163m, 3061m, 2987m, 1773m, 1700m, 1635m, 1500m, 1479m, 1259s (P=O), 1184m,
1053s/1028s (P-O-C), 768m, 698m, 525m. $^1$H-NMR (250.13 MHz, CDCl$_3$): $\delta$ [ppm] = 7.81-7.36 (m, 10 H, arom. H), 4.26-4.07 (m, 4H, P-O-CH$_2$-CH$_3$), 2.65 (s, 3H, CH$_3$ at C-7), 1.24-1.18 (m, 6H, P-O-CH$_2$-CH$_3$). $^{13}$C-NMR (62.89 MHz, CDCl$_3$): $\delta$ [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), 71.74 (s, C-8), 63.76 (d, $^3$J$_{CP}$ = 6.2 Hz, P-O-CH$_2$-CH$_3$), 16.11 (d, $^3$J$_{CP}$ = 6.7 Hz, P-O-CH$_2$-CH$_3$), 13.73 (s, CH$_3$ at C-7).

El-MS: m/z (%) = 447 (25, [M+1]$^+$), 446 (89, [M]$^+$), 373 (11, [M-C$_2$H$_5$O-C$_2$H$_4$]$^+$), 338 (14), 337 (24), 310 (35), 309 (56, [M-PO(OC$_3$H$_7$)$_2$]$^+$), 165 (10), 140 (23), 139 (100), 102 (17), 81 (13), 77 (11).

HR-MS: m/z Calcd for C$_{24}$H$_{23}$N$_4$O$_3$P: 446.1508. Found: 446.1508. Anal. Calcd for C$_{24}$H$_{23}$N$_4$O$_3$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-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$_2$O for 3 h and in n-hexane for 24 h as a yellow solid; yield: 80 mg (38 %), mp 207 °C. UV/VIS (CH$_2$Cl$_2$): $\lambda$ (log $\varepsilon$) = 232 (4.42), 280 (4.14), 308 (4.08), 380 (4.02). IR (KBr): $\nu$ [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. $^1$H-NMR (250.13 MHz, CDCl$_3$): $\delta$ [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-(CH$_3$)$_2$), 2.62 (s, 3H, CH$_3$ at C-7), 1.38 (d, 6H, $^3$J$_{HH}$ = 6.1 Hz, P-O-CH-(CH$_3$)$_2$), 1.32 (d, 6H, $^3$J$_{HH}$ = 6.1 Hz, P-O-CH-(CH$_3$)$_2$). $^{13}$C-NMR (62.89 MHz, CDCl$_3$): $\delta$ [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-CH-(CH$_3$)$_2$), 24.00-23.73 (m, P-O-CH-(CH$_3$)$_2$), 13.44 (s, CH$_3$ at

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