SYNTHESIS AND REACTIONS OF DIALKYL (1-*R*-5-AMINO-3-METHYLSULFANYL-1*H*-PYRAZOL-4-YL)PHOSPHONATES

Harald G. Krug,[a)] Richard Neidlein,[a)*] Roland Boese,[b)] and Walter Kramer [a)]

a) Pharmazeutisch-Chemisches Institut, Im Neuenheimer Feld 364, 69120 Heidelberg, Germany

b) Institut für Anorganische Chemie, Universitätsstraße 5-7, 45117 Essen, Germany

Abstract - Dialkyl (1-cyano-2,2-bismethylsulfanylvinyl)phosphonates (**2**) react with hydrazines (**4**) to yield pyrazoles (**5**). The composition of one reaction product is examined by X-ray crystal structure analysis. *N*-Unsubstituted pyrazoles (**5a**) treated with 1,3-diketones (**6**) give pyrazolo[1,5-*a*]pyrimidines (**7**).

Introduction

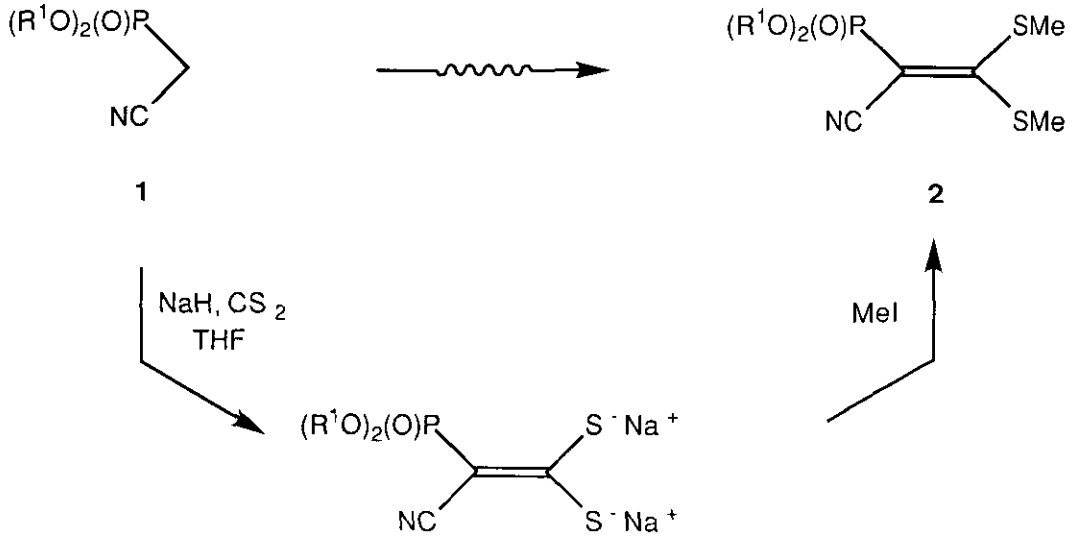
Research into organophosphorus compounds has been stimulated during the last years, because some phosphorus containing compounds have been reported to possess antibacterial, antibiotic, antineoplastic or antiviral activity.[1] For this reason, the synthesis of phosphono-substituted heterocycles was extensively studied by us.[2-9] Phosphono-substituted pyrazoles should be of an interest, because numerous pyrazoles show biological activity and some are even used as drugs.[10,11] Dialkyl (1-cyano-2,2-bismethylsulfanylvinyl)phosphonates (**2**) should be useful starting compounds for the preparation of phosphono-substituted pyrazoles because of the high reactivity expected from these ketene-S,S-acetals.

The present paper describes the results of our studies concerning the preparation and reactions of

dialkyl (1-*R*-5-amino-3-methylsulfanyl-1*H*-pyrazol-4-yl)phosphonates (**5**).

Results and Discussion

Diethyl (1-cyano-2,2-bismethylsulfanylvinyl)phosphonate (**2.1**) was first prepared by E. Schaumann and F.-F. Grabley[12] (yield: 40 %). We used a modification of their method to prepare compound (**2.1**) as well as the unknown diisopropyl ester (**2.2**) (Scheme 1). The starting materials (**1**) were obtained in good yields from the corresponding trialkylphosphite by treatment of the preceeding with chloroacetonitrile[13] (4 h, reflux). When treated with sodium hydride, the methylene activated dialkyl cyanomethylphosphonates (**1**) led to the corresponding sodium salts. These in turn, underwent addition of carbon disulfide in the presence of a further equimolar amount of sodium hydride yielding the disodium salts (**3**).

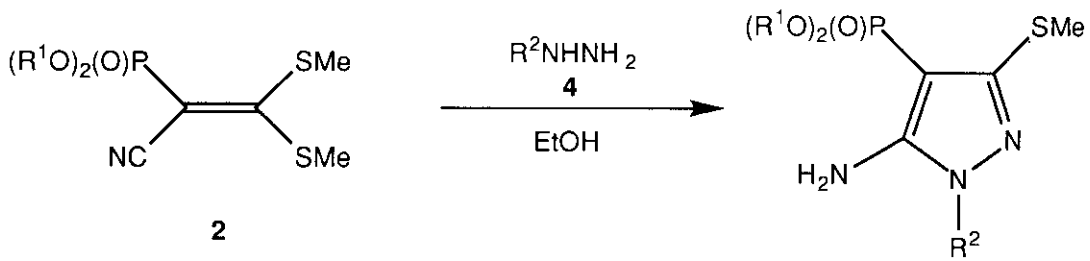


Compound	R^1
2.1	Et
2.2	^{i}Pr

Scheme 1: Synthesis of ketene-S,S-acetals (**2**)

Compounds (**3**) were not isolated but directly treated with methyl iodide (1 h, reflux). The crude products (**2**) were chromatographed on silica gel (ethyl acetate / hexane (1:1)) and isolated in good yields (68 - 76 %).

Hydrazines (**4**) reacted with the dialkyl (1-cyano-2,2-bismethylsulfanylvinyl)phosphonates (**2**) in ethanol to give the phosphono-substituted pyrazoles (**5**) (Scheme 2). All compounds (**5**) were isolated as colorless crystals with the exception of product (**5.2b**), which was obtained as a viscous oil. The reaction conditions and the purification of the crude products (**5**) depended to a great extent on the hydrazines (**4**) used (yields: 72 - 91 %).



2 **5**

Compound	R^1	R^2
5.1a	Et	H
5.1b	Et	Ph
5.1c	Et	Pyridin-2-yl
5.1d	Et	6-Chloropyridin-2-yl
5.1e	Et	Pyrazin-2-yl
5.1f	Et	6-Chloropyridazin-3-yl
5.2a	^{i}Pr	H
5.2b	^{i}Pr	Ph

Scheme 2: Synthesis of pyrazoles (**5**)

The structure of the pyrazoles (**5**) was investigated by nmr spectroscopy (nOe-measurements) and X-ray analysis.

The lack of nOe between H-3' and NH_2 in **5.1c** (Figure 1) can be explained by a preferred conformation due to intramolecular hydrogen bonding between one of the NH_2-protons and the pyridine-nitrogen atom N-1'. Therefore, H-3' is too far from NH_2 to give an observable nOe even with the difference spectroscopy technique. However, in compound (**5.1e**) this is not the case.

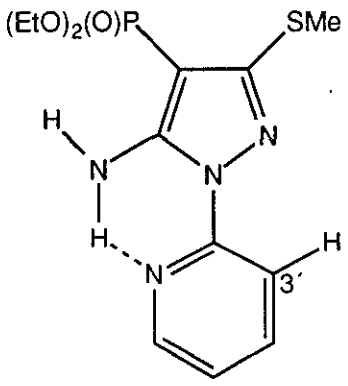


Figure 1: Compound (**5.1c**)

In compound (**5.1e**) nOes occur at the NH_2- and SCH_3-protons upon irradiation of H-3' even though the rotation of the six-membered ring is hindered. The X-ray structure (Figure 2) favors the hydrogen bonded confirmation (as shown in Figure 1) in the solid state; however, other conformations may exist in solution. The observed nOes provide clear evidence that besides this conformation others in solution must be taken into account, such as the isomer which exists at room temperature when H-3' is in the neighborhood of the NH_2 group.

Spectroscopic evidence for the presence of intramolecular hydrogen bonds between one of the hydrogens of the NH_2-group and the nearby pyridine- and pyrazine-nitrogen atoms in **5.1c** and **5.1e** is given by different chemical shifts of the NH_2-protons in each molecule at low temperatures (**5.1c**: NH_a = 8.44 ppm, NH_b = 6.98 ppm, **5.1e**: NH_a = 8.10 ppm, NH_b = 7.08 ppm at 213 K in acetone-d_6) but there is no significant difference in the estimated $G^{\#}$-values[14] at the individual coalescense temperatures (**5.1c**: T_c = 242 K, **5.1e**: T_c = 232 K).

To obtain further structural information, an X-ray crystal structure analysis of **5.1e** was performed.

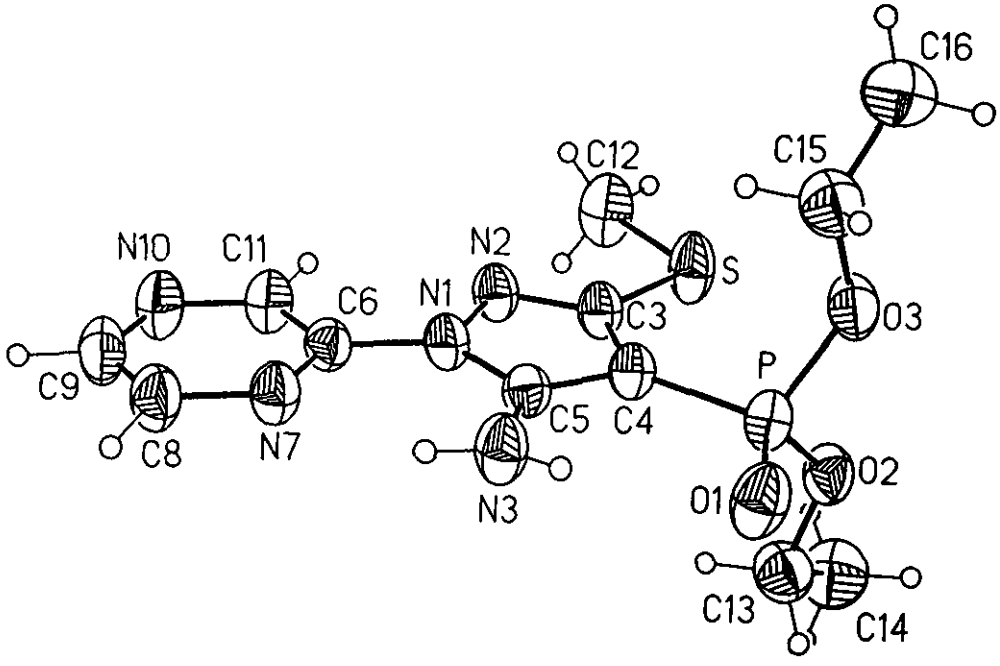


Figure 2: Perspective view and atom labelling of the crystal structure of **5.1e** (50 % ellipsoids)

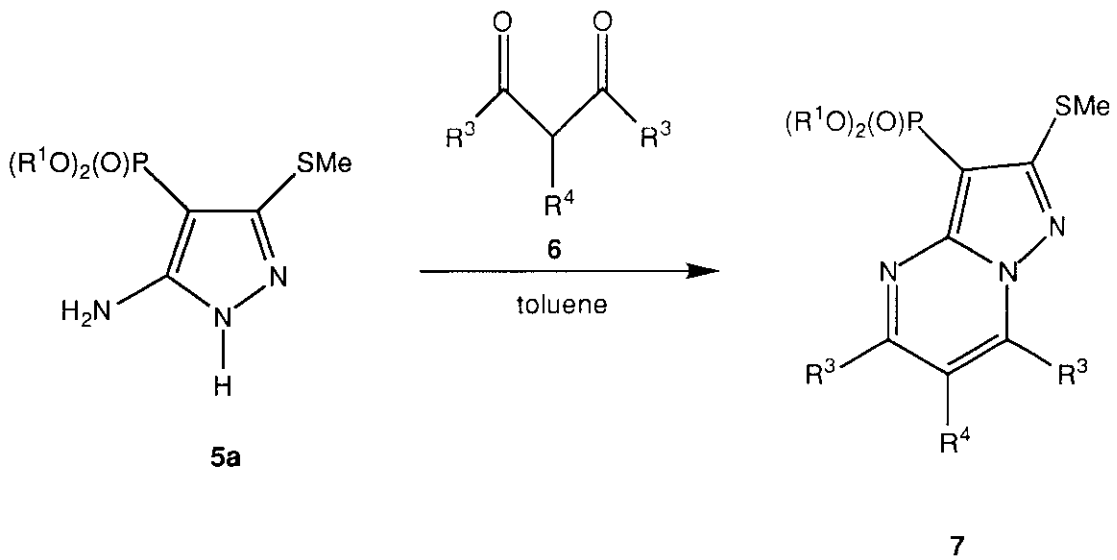
As seen from Figure 2, compound (**5.1e**) is nearly planar with the exception of the ethoxy group of the phosphono-substituent and the hydrogen atoms of the methylsulfanyl group.

In the pyrazole ring of **5.1e**, the N1-N2, N1-C5 and C4-C5 distances (1.395 (2) Å, 1.370 (2) Å and 1.401 (2) Å) are longer than the corresponding values of 1*H*-pyrazole (1.366 Å, 1.357 Å and 1.369 Å).[15] The C3-C4 bond length (1.419 (3) Å) is in accordance with the value described in the literature (1.410 Å),[15] while the N2-C3 distance (1.310 (2) Å) is somewhat shorter than that of 1*H*-pyrazole (1.329 Å).[15]

There is no evidence of intra- or intermolecular hydrogen bonding (the N3···O1 distance is 2.895 Å which is outside the range assuming significant interaction, the C4-P-O angles are almost equal). The molecules are packed pairwise with S···S contacts (3.554 Å) *via* the crystallographic inversion center.

In summary the X-ray structure analysis confirms the generation of the pyrazole ring with substitution as indicated.

Pyrazoles (**5a**) were cyclized to the phosphono-substituted pyrazolo[1,5-*a*]pyrimidines (**7**) (Scheme 3) by refluxing with 1,3-diketones (**6**) in anhydrous toluene (3 - 10 h, yield: 68 - 98 %).



Compound	R^1	R^3	R^4
7.1m	Et	Me	H
7.1n	Et	Me	Me
7.1o	Et	Ph	H
7.2m	^{i}Pr	Me	H
7.2n	^{i}Pr	Me	Me

Scheme 3: Synthesis of pyrazolo[1,5-*a*]pyrimidines (**7**)

In summary, ketene-S,S-acetals (**2**) are useful starting materials for phosphono-substituted pyrazoles (**5**), which are easily available in good yields. Phosphono-substituted pyrazoles (**5a**) can be cyclized to pyrazolo[1,5-*a*]pyrimidines (**7**).

EXPERIMENTAL

Melting points were determined on a Reichert hot stage microscope and are uncorrected. Infrared spectra were measured with a Perkin-Elmer ir-spectrophotometer 1600 (FTIR) and are given as cm^{-1}. ^1H- and ^{13}C-nmr spectra were recorded on either a Bruker WM-250 (^1H-nmr: 250.13 MHz, ^{13}C-nmr: 62.89 MHz) or a Varian XL 300 (^1H-nmr: 299.95 MHz, ^{13}C-nmr: 75.43 MHz) spectrometer. The chemical shifts are reported in parts per million (ppm) downfield from internal tetramethylsilane; coupling constants J are given in Hz. ^{31}P-nmr spectra were measured on the Varian XL 300 (^{31}P-nmr: 121.42 MHz) spectrometer using H_3PO_4 as external standard. Ultraviolet spectra were recorded with a Perkin-Elmer 320 uv-spectrophotometer and elementary analyses were performed on a Heraeus Vario EL CHNS apparatus. P- and Cl-analyses were conducted by the Department of Chemistry at the University of Heidelberg.

Diethyl (1-cyano-2,2-bismethylsulfanylvinyl)phosphonate (**2.1**) was prepared in the same way as compound (**2.2**) (yield: 68 %) and its spectroscopic data is identical with that reported in the literature.[12] (6-Chloropyridin-2-yl)hydrazine (**4d**),[16] (pyrazin-2-yl)hydrazine (**4e**)[17] and (6-chloropyridazin-3-yl)hydrazine (**4f**)[18] were prepared according to the literature.

Diisopropyl (1-cyano-2,2-bismethylsulfanylvinyl)phosphonate (**2.2**)

Diisopropyl cyanomethylphosphonate (**1.2**) (41.0 g, 200 mmol) was slowly added at room temperature to a stirred suspension of sodium hydride (9.60 g, 400 mmol) in anhydrous tetrahydrofuran (700 ml) under argon. Vigorous evolution of hydrogen was observed. After the addition was completed, the suspension was stirred for 90 min at room temperature. A solution of carbon disulfide (15.2 g, 200 mmol) in anhydrous tetrahydrofuran (40 ml) was added dropwise and the yellow suspension was vigorously stirred for 3 h at room temperature. A solution of methyl iodide (56.8 g, 400 mmol) in anhydrous tetrahydrofuran (80 ml) was added and the suspension was refluxed for 90 min. The reaction mixture was cooled to room temperature and water (200 ml) was added. The resulting solution was extracted with chloroform (3 x 100 ml). The combined organic layers were dried with anhydrous magnesium sulfate and filtered. After the evaporation of the solvents, the crude product was chromatographed on silica gel (ethyl acetate / hexane (1:1)).

47.2 g (76 %) **2.2**, pale yellow oil. ^{1}H-Nmr (299.95 MHz, $CDCl_3$) δ = 1.39 (d, $^3J_{HH}$ = 6.2 Hz, 12H, OCH($C\underline{H}_3$)$_2$), 2.61, 2.68 (2 * s, 2 * 3H, SCH_3), 4.78 (dseptet, $^3J_{HH}$ = 6.2 Hz, $^3J_{PH}$ = 7.7 Hz, 2H, O$C\underline{H}$(CH_3)$_2$). ^{13}C-Nmr (75.43 MHz, $CDCl_3$, {^{1}H}) δ = 19.2, 19.7 (2 * s, SCH_3), [23.7 (d, $^3J_{PC}$ = 6 Hz), 24.0 (d, $^3J_{PC}$ = 5 Hz); OCH($\underline{C}H_3$)$_2$], 72.6 (d, $^2J_{PC}$ = 6 Hz, O$\underline{C}$H(CH_3)$_2$), 100.1 (d, $^1J_{PC}$ = 201 Hz, C-1), 116.3 (d, $^2J_{PC}$ = 11 Hz, CN), 179.2 (d, $^2J_{PC}$ = 9 Hz, C-2). ^{31}P-Nmr (121.42 MHz, $CDCl_3$) δ = 5.8 (s). Ir (NaCl, film) ν = 2980 (m), 2930 (w), 2200 (w), 1465 (m), 1430 (w), 1385 (w), 1375 (w), 1255 (m), 1180 (w), 1140 (w), 1130 (w), 1105 (m), 990 (s), 940 (w), 900 (w), 885 (w), 670 (w). Uv (MeCN) λ_{max} (lg ε) = 220 (3.66), 321 (4.08). *Anal.* Calcd for $C_{11}H_{20}NO_3PS_2$: C, 42.70; H, 6.52; N, 4.53. Found: C, 42.90; H, 6.48; N, 4.82.

Diethyl (5-amino-3-methylsulfanyl-1*H*-pyrazol-4-yl)phosphonate (**5.1a**)

Diethyl (1-cyano-2,2-bismethylsulfanylvinyl)phosphonate (**2.1**) (1.41 g, 5.00 mmol) and 100 % hydrazine hydrate (**4a**) (250 mg, 5.00 mmol) were stirred in ethanol (5 ml) at room temperature for 2.5 h. The solvent was removed under reduced pressure and the resulting crude product washed with ether. 1.13 g (85 %) **5.1a**, colorless crystals, mp 123 - 124 °C. ^{1}H-Nmr (299.95 MHz, acetone-d_6) δ = 1.28 (dt, $^3J_{HH}$ = 7.1 Hz, $^4J_{PH}$ = 0.5 Hz, 6H, $OCH_2C\underline{H}_3$), 2.43 (s, 3H, SCH_3), 3.94 - 4.04 (m, 4H, $OC\underline{H}_2CH_3$), 5.66 (*br s*, 2H, NH_2). ^{13}*C-Nmr* (*75.43 MHz, acetone-d_6,* {^{1}H}) δ = 13.7 (s, SCH_3), 16.6 (d, $^3J_{PC}$ = 7 Hz, $OCH_2\underline{C}H_3$), 61.8 (d, $^2J_{PC}$ = 4 Hz, O$\underline{C}$H$_2$CH$_3$), 84.1 (d, $^1J_{PC}$ = 222 Hz, C-4), 148.6 (d, $^2J_{PC}$ = 12 Hz, C-3), 157.0 (d, $^2J_{PC}$ = 22 Hz, C-5). ^{31}P-Nmr (121.42 MHz, acetone-d_6) δ = 16.7 (s). Ir (KBr, tablet) ν = 3430 (m), 3340 (m), 3210 (m), 3130 (m), 2980 (m), 2930 (w), 2910 (w), 1655 (w), 1610 (s), 1575 (m), 1495 (m), 1435 (w), 1390 (w), 1300 (m), 1225 (s), 1180 (m), 1095 (w), 1045 (s), 1020 (s), 960 (s), 820 (w), 795 (w), 775 (m), 740 (w), 720 (w), 605 (m). Uv (MeCN) λ_{max} (lg ε) = 211 (4.17), 240 (3.43, sh). *Anal.* Calcd for $C_8H_{16}N_3O_3PS$: C, 36.22; H, 6.08; N, 15.84; P, 11.68; S, 12.09. Found: C, 36.39; H, 5.99; N, 15.72; P, 11.61; S, 12.37.

Diethyl (5-amino-3-methylsulfanyl-1-phenyl-1*H*-pyrazol-4-yl)phosphonate (**5.1b**)

Compound (**2.1**) (1.41g, 5.00 mmol) and phenylhydrazine (**4b**) (541 mg, 5.00 mmol) were stirred in ethanol (5 ml) at room temperature for 2 h. After the evaporation of the solvent under reduced

pressure, the resulting oil was treated with ether / pentane (1 : 2). The product (**5.1b**) crystallized after storage at -30 °C, *ca.* 12 h. 1.54 g (90 %) **5.1b**, colorless crystals, mp 87 °C. ^{1}H-Nmr (299.95 MHz, $CDCl_3$) δ = 1.37 (t, $^3J_{HH}$ = 7.1 Hz, 6H, $OCH_2\underline{C}H_3$), 2.54 (s, 3H, SCH_3), 4.07 - 4.18 (m, 4H, $OC\underline{H}_2CH_3$), 5.26 (br s, 2H, NH_2), 7.36 - 7.56 (m, 5H, H_{ar}). ^{13}C-Nmr (75.43 MHz, $CDCl_3$, {^{1}H}) δ = 13.6 (s, SCH_3), 16.3 (d, $^3J_{PC}$ = 7 Hz, $OCH_2\underline{C}H_3$), 61.9 (d, $^2J_{PC}$ = 4 Hz, $O\underline{C}H_2CH_3$), 84.7 (d, $^1J_{PC}$ = 222 Hz, C-4), 123.6, 127.6, 129.5 (3 * s, C-2' - C-6'), 137.5 (s, C-1'), 149.8 (d, $^2J_{PC}$ = 10 Hz, C-3), 153.1(d, $^2J_{PC}$ = 23 Hz, C-5). ^{31}P-Nmr (121.42 MHz, $CDCl_3$) δ = 15.1 (s). Ir (KBr, tablet) ν = 3400 (m), 3280 (m), 3200 (m), 2990 (m), 2920 (w), 2910 (w), 1625 (m), 1600 (m), 1540 (m), 1535 (m), 1515 (s), 1475 (w), 1455 (m), 1440 (w), 1390 (w), 1355 (m), 1315 (w), 1285 (w), 1225 (m), 1210 (m), 1180 (m), 1105 (w), 1075 (m), 1050 (m), 1025 (s), 975 (s), 960 (m), 805 (w), 780 (m), 775 (m), 700 (m), 605 (m), 575 (m). Uv (MeCN) λ_{max} (lg ε) = 222 (4.31), 260 (3.88, sh). *Anal.* Calcd for $C_{14}H_{20}N_3O_3PS$: C, 49.26; H, 5.91; N, 12.31; P, 9.07; S, 9.39. Found: C, 49.10; H, 5.92; N, 12.06; P, 9.04; S, 9.47.

Diethyl (5-amino-3-methylsulfanyl-1-pyridin-2-yl-1*H*-pyrazol-4-yl)phosphonate (**5.1c**)

Compound (**2.1**) (1.41 g, 5.00 mmol) and (pyridin-2-yl)hydrazine (**4c**) (546 mg, 5.00 mmol) were stirred in ethanol (5 ml) at room temperature for 2 h. The solvent was removed under reduced pressure and the crude product chromatographed on silica gel (ethyl acetate). 1.36 g (79 %) **5.1c**, colorless crystals, mp 71 °C. ^{1}H-Nmr (250.13 MHz, $CDCl_3$) δ = 1.36 (t, $^3J_{HH}$ = 7.1 Hz, 6H, $OCH_2\underline{C}H_3$), 2.58 (s, 3H, SCH_3), 4.00 - 4.18 (m, 4H, $OC\underline{H}_2CH_3$), 7.07 - 7.13 (m, 1H, H-5'), 7.42 (br s, 2H, NH_2), 7.75 - 7.92 (m, 2H, H-3', H-4'), 8.32 - 8.34 (m, 1H, H-6'). ^{13}C-Nmr (62.89 MHz, $CDCl_3$, {^{1}H}) δ = 13.3 (s, SCH_3), 16.3 (d, $^3J_{PC}$ = 7 Hz, $OCH_2\underline{C}H_3$), 61.9 (d, $^2J_{PC}$ = 4 Hz, $O\underline{C}H_2CH_3$), 83.5 (d, $^1J_{PC}$ = 222 Hz, C-4), 113.3 (s, C-3'), 119.7 (s, C-5'), 138.7 (s, C-4'), 146.6 (s, C-6'), 151.4 (d, $^2J_{PC}$ = 10 Hz, C-3), 154.1 (s, C-2'), 156.3 (d, $^2J_{PC}$ = 24 Hz, C-5). ^{31}P-Nmr (121.42 MHz, $CDCl_3$) δ = 14.9 (s). Ir (KBr, tablet) ν = 3420 (m), 3310 (m), 2980 (m), 2930 (m), 2900 (m), 1735 (w), 1720 (w), 1685 (w), 1655 (w), 1590 (s), 1520 (m), 1490 (m), 1465 (s), 1440 (s), 1360 (m), 1290 (m), 1230 (m), 1180 (m), 1025 (s), 955 (m), 800 (w), 785 (m), 770 (m), 740 (w), 725 (w), 705 (m), 630 (w), 610 (m), 530 (w). Uv (MeCN) λ_{max} (lg ε) = 216 (4.23), 227 (4.11, sh),

261 (4.19), 288 (3.99, sh). *Anal.* Calcd for $C_{13}H_{19}N_4O_3PS$: C, 45.61; H, 5.59; N, 16.37; P, 9.05; S, 9.37. Found: C, 45.75; H, 5.63; N, 16.23; P, 8.88; S, 9.60.

Diethyl [5-amino-1-(6-chloropyridin-2-yl)-3-methylsulfanyl-1*H*-pyrazol-4-yl]phosphonate (**5.1d**)

Compound (**2.1**) (1.41g, 5.00 mmol) and (6-chloropyridin-2-yl)hydrazine (**4d**) (718 mg, 5.00 mmol) were refluxed in ethanol (5 ml) for 3 h. The solvent was removed under reduced pressure and the crude product chromatographed on silica gel (ethyl acetate / hexane (3:4)). 1.65 g (87 %) **5.1d**, colorless crystals, mp 104 °C. ^{1}H-Nmr (299.95 MHz, $CDCl_3$) δ = 1.36 (t, $^3J_{HH}$ = 7.1 Hz, 6H, $OCH_2C\underline{H}_3$), 2.57 (s, 3H, SCH_3), 4.01 - 4.15 (m, 4H, $OC\underline{H}_2CH_3$), 7.10 - 7.13 (m, 1H, H-5'), 7.24 (br s, 2H, NH_2), 7.71 - 7.82 (m, 2H, H-3', H-4'). ^{13}C-Nmr (75.43 MHz, $CDCl_3$, {^{1}H}) δ = 13.2 (s, SCH_3), 16.3 (d, $^3J_{PC}$ = 7 Hz, $OCH_2\underline{C}H_3$), 61.9 (d, $^2J_{PC}$ = 4 Hz, $O\underline{C}H_2CH_3$), 83.8 (d, $^1J_{PC}$ = 221 Hz, C-4), 111.2 (s, C-3'), 119.4 (s, C-5'), 140.7 (s, C-4'), 148.0 (s, C-6'), 152.0 (d, $^2J_{PC}$ = 11 Hz, C-3), 153.0 (s, C-2'), 155.9 (d, $^2J_{PC}$ = 24 Hz, C-5). ^{31}P-Nmr (121.42 MHz, $CDCl_3$) δ = 15.0 (s). Ir (KBr, tablet) ν = 3430 (m), 3320 (m), 2990 (w), 2930 (w), 1635 (w), 1605 (s), 1585 (m), 1530 (m), 1485 (s), 1445 (s), 1415 (m), 1400 (m), 1360 (w), 1295 (m), 1215 (m), 1190 (m), 1160 (w), 1120 (w), 1100 (w), 1050 (m), 1030 (s), 990 (w), 955 (m), 790 (m), 770 (w), 760 (w), 735 (w), 675 (w), 615 (m). Uv (MeCN) λ_{max} (lg ε) = 218 (4.44), 266 (4.22), 288 (4.09, sh). *Anal.* Calcd for $C_{13}H_{18}N_4O_3ClPS$: C, 41.44; H, 4.82; N, 14.87; Cl, 9.41; P, 8.22; S, 8.51. Found: C, 41.71; H, 4.84; N, 14.89; Cl, 9.52; P, 8.19; S, 8.60.

Diethyl (5-amino-3-methylsulfanyl-1-pyrazin-2-yl-1*H*-pyrazol-4-yl)phosphonate (**5.1e**)

Compound (**2.1**) (1.41 g, 5.00 mmol) and (pyrazin-2-yl)hydrazine (**4e**) (551 mg, 5.00 mmol) were refluxed in ethanol (5 ml) for 3 h. The reaction mixture was cooled to -30 °C and the crystals which separated were isolated by filtration. The crude product was recrystallized from ethyl acetate. 1.39 g (81 %) **5.1e**, colorless crystals, mp 113 °C (ethyl acetate). ^{1}H-Nmr (299.95 MHz, $CDCl_3$) δ = 1.37 (t, $^3J_{HH}$ = 7.1 Hz, 6H, $OCH_2C\underline{H}_3$), 2.60 (s, 3H, SCH_3), 4.04 - 4.16 (m, 4H, $OC\underline{H}_2CH_3$), 7.25 (br s, 2H, NH_2), 8.28 (dd, $^3J_{HH}$ = 2.7 Hz, $^5J_{HH}$ = 1.5 Hz, 1H, H-6'), 8.40 (d, $^3J_{HH}$ = 2.7 Hz, 1H, H-5'), 9.26 (d, $^5J_{HH}$ = 1.5 Hz, 1H, H-3'). ^{13}C-Nmr (75.43 MHz, $CDCl_3$, {^{1}H}) δ = 13.2 (s, SCH_3),

16.3 (d, $^{3}J_{PC}$ = 7 Hz, $OCH_2\underline{C}H_3$), 62.0 (d, $^{2}J_{PC}$ = 4 Hz, $O\underline{C}H_2CH_3$), 83.8 (d, $^{1}J_{PC}$ = 221 Hz, C-4), 136.4, 139.6, 139.8 (3 *s, C-3', C-5', C-6'), 149.4 (s, C-2'), 152.7 (d, $^{2}J_{PC}$ = 11 Hz, C-3), 156.5 (d, $^{2}J_{PC}$ = 24 Hz, C-5). ^{31}P-Nmr (121.42 MHz, $CDCl_3$) δ = 14.8 (s). Ir (KBr, tablet) ν = 3420 (m), 3310 (m), 2980 (m), 2950 (w), 2930 (w), 2900 (w), 1595 (m), 1575 (m), 1560 (w), 1535 (m), 1515 (m), 1485 (m), 1470 (m), 1430 (s), 1390 (m), 1370 (w), 1350 (w), 1310 (m), 1295 (w), 1230 (m), 1185 (w), 1170 (m), 1115 (w), 1080 (w), 1025 (s), 1010 (m), 975 (s), 960 (m), 840 (w), 805 (m), 790 (m), 595 (w), 500 (w). Uv (MeCN) λ_{max} (lg ε) = 216 (4.46, sh), 271 (4.20), 310 (3.78, sh). *Anal.* Calcd for $C_{12}H_{18}N_5O_3PS$: C, 41.98; H, 5.28; N, 20.40; P, 9.02; S, 9.34. Found: C, 42.07; H, 5.27; N, 20.18; P, 9.04; S, 9.24.

Colorless crystals of **5.1e** with the space group $P\bar{1}$ (# 2 Int. Tables) were obtained by recrystallization from ethyl acetate: $C_{12}H_{18}N_5O_3PS$, mol. weight = 343.35 g mol^{-1}, ρ_{calcd} = 1.426 g cm^{-3}, a = 8.293 (2) Å, b = 8.547 (1) Å, c = 12.628 (2) Å, α = 106.81 (1) °, β = 95.32 (2) °, γ = 107.79 (1) °, V = 799.6 (3) $Å^3$, μ = 3.2 cm^{-1} (MoKα), Z = 2 (no absorption correction was applied).

A total of 2815 unique intensities were recorded, of which 2459 were observed ($F_o \geq 4\sigma(F)$) on a Siemens P4 diffractometer using a graphite-monochromated Mo-Kα radiation (λ = 0.71069 Å).

The structure was solved by direct phase determination methods and refined with isotropic hydrogen atoms as riding groups, 225 parameters (SHELXTL-PLUS by G. M. Sheldrick) on a SGI IRIS Indigo to a final R = 0.0360, R_w = 0.0443, maximum residual electron density 0.27 e $Å^{-3}$.

Further details of the crystal structure investigation are available on request from the Fachinformationszentrum Energie Physik Mathematik, Leopoldshafen 2, 76344 Eggenstein, Germany, on quoting the depository number CSD 401219, the author names, and the full citation of the journal.

Table 1: Atomic coordinates ($x10^4$) and equivalent isotropic displacement coefficients ($Å^2x10^3$) of **5.1e**

Atom	x	y	z	U (eq)
S	4527 (1)	11611 (1)	1041 (1)	66 (1)*
P	2737 (1)	8070 (1)	1993 (1)	48 (1)*
O(1)	1775 (2)	7039 (2)	2622 (1)	68 (1)*
O(2)	1982 (2)	7485 (2)	699 (1)	56 (1)*
O(3)	4547 (2)	7914 (2)	1840 (1)	60 (1)*
N(1)	2909 (2)	12699 (2)	3809 (1)	45 (1)*
N(2)	3654 (2)	13190 (2)	2955 (1)	49 (1)*
C(3)	3695 (2)	11730 (2)	2268 (1)	47 (1)*
C(4)	3004 (2)	10266 (2)	2616 (1)	45 (1)*
C(5)	2513 (2)	10953 (2)	3632 (1)	43 (1)*
N(3)	1805 (2)	10159 (2)	4328 (1)	58 (1)*
C(6)	2560 (2)	13954 (2)	4652 (1)	45 (1)*
N(7)	1873 (2)	13468 (2)	5456 (1)	54 (1)*
C(8)	1517 (3)	14688 (3)	6243 (2)	61 (1)*
C(9)	1879 (3)	16337 (3)	6217 (2)	66 (1)*
N(10)	2577 (3)	16835 (2)	5401 (2)	65 (1)*
C(11)	2910 (3)	15643 (2)	4618 (2)	57 (1)*
C(12)	5132 (4)	13815 (3)	1082 (2)	78 (1)*
C(13)	325 (3)	7518 (3)	292 (2)	70 (1)*
C(14)	203 (4)	7391 (4)	-918 (2)	86 (1)*
C(15)	5907 (3)	8480 (3)	2818 (2)	66 (1)*
C(16)	7572 (3)	8755 (4)	2409 (2)	82 (1)*

*) Equivalent isotropic U defined as one third of the trace of the orthogonalized U_{ij} tensor

Table 2: Bond lengths (Å) of **5.1e**

S–C(3)	1.743 (2)	S–C(12)	1.780 (3)
P–O(1)	1.461 (2)	P–O(2)	1.569 (1)
P–O(3)	1.571 (2)	P–C(4)	1.747 (2)
O(2)–C(13)	1.433 (3)	O(3)–C(15)	1.447 (2)
N(1)–N(2)	1.395 (2)	N(1)–C(5)	1.370 (2)
N(1)–C(6)	1.398 (2)	N(2)–C(3)	1.310 (2)
C(3)–C(4)	1.419 (3)	C(4)–C(5)	1.401 (2)
C(5)–N(3)	1.332 (3)	C(6)–N(7)	1.317 (3)
C(6)–C(11)	1.398 (3)	N(7)–C(8)	1.344 (3)
C(8)–C(9)	1.359 (3)	C(9)–N(10)	1.338 (3)
N(10)–C(11)	1.316 (3)	C(13)–C(14)	1.491 (4)
C(15)–C(16)	1.494 (4)		

Table 3: Bond angles (°) of **5.1e**

C(3)–S–C(12)	101.3 (1)	O(1)–P–O(2)	116.6 (1)
O(1)–P–O(3)	116.0 (1)	O(2)–P–O(3)	95.3 (1)
O(1)–P–C(4)	110.1 (1)	O(2)–P–C(4)	108.9 (1)
O(3)–P–C(4)	109.0 (1)	P–O(2)–C(13)	121.7 (1)
P–O(3)–C(15)	120.0 (1)	N(2)–N(1)–C(5)	112.2 (1)
N(2)–N(1)–C(6)	118.4 (1)	C(5)–N(1)–C(6)	129.3 (2)
N(1)–N(2)–C(3)	103.7 (1)	S–C(3)–N(2)	122.7 (2)
S–C(3)–C(4)	123.4 (1)	N(2)–C(3)–C(4)	113.9 (2)
P–C(4)–C(3)	131.4 (1)	P–C(4)–C(5)	124.6 (1)
C(3)–C(4)–C(5)	104.1 (1)	N(1)–C(5)–C(4)	106.2 (2)
N(1)–C(5)–N(3)	124.1 (2)	C(4)–C(5)–N(3)	129.8 (2)
N(1)–C(6)–N(7)	117.4 (2)	N(1)–C(6)–C(11)	120.4 (2)
N(7)–C(6)–C(11)	122.2 (2)	C(6)–N(7)–C(8)	116.2 (2)
N(7)–C(8)–C(9)	121.6 (2)	C(8)–C(9)–N(10)	122.4 (2)
C(9)–N(10)–C(11)	116.5 (2)	C(6)–C(11)–N(10)	121.2 (2)
O(2)–C(13)–C(14)	108.4 (2)	O(3)–C(15)–C(16)	107.0 (2)

Diethyl [5-amino-1-(6-chloropyridazin-3-yl)-3-methylsulfanyl-1*H*-pyrazol-4-yl]phosphonate (**5.1f**)

Compound (**2.1**) (1.41 g, 5.00 mmol) and (6-chloropyridazin-3-yl)hydrazine (**4f**) (723 mg, 5.00 mmol) were refluxed in ethanol (5 ml) for 4 h. The solvent was removed under reduced pressure and the semicrystalline product chromatographed on silica gel (ethyl acetate / hexane (2:1)). 1.37 g (72 %) **5.1f**, colorless crystals, mp 131 °C. ^{1}H-Nmr (299.95 MHz, $CDCl_3$) δ = 1.37 (t, $^3J_{HH}$ = 7.1 Hz, 6H, $OCH_2\underline{C}H_3$), 2.56 (s, 3H, SCH_3), 4.05 - 4.16 (m, 4H, $OC\underline{H}_2CH_3$), 7.44 (br s, 2H, NH_2), 7.61 (d, $^3J_{HH}$ = 9.3 Hz, 1H, H-5'), 8.13 (d, $^3J_{HH}$ = 9.3 Hz, 1H, H-4'). ^{13}C-Nmr (75.43 MHz, $CDCl_3$, {^{1}H}) δ = 13.2 (s, SCH_3), 16.3 (d, $^3J_{PC}$ = 7 Hz, $OCH_2\underline{C}H_3$), 62.0 (d, $^2J_{PC}$ = 5 Hz, $O\underline{C}H_2CH_3$), 84.2 (d, $^1J_{PC}$ = 222 Hz, C-4), 120.9 (s, C-4'), 130.5 (s, C-5'), 152.5, 156.2 (2 •s, C-3', C-6'), 153.5 (d, $^2J_{PC}$ = 10 Hz, C-3), 156.1 (d, $^2J_{PC}$ = 24 Hz, C-5). ^{31}P-Nmr (121.42 MHz, $CDCl_3$) δ = 13.9 (s). Ir (KBr, tablet) ν = 3430 (m), 3320 (m), 2980 (w), 2930 (w), 2910 (w), 1605 (s), 1575 (m), 1545 (m), 1520 (m), 1485 (m), 1425 (s), 1360 (m), 1295 (w), 1210 (m), 1180 (m), 1160 (w), 1140 (w), 1090 (w), 1055 (m), 1025 (s), 980 (w), 955 (s), 935 (m), 845 (w), 815 (w), 795 (m), 760 (m), 750 (w), 635 (m), 615 (m), 550 (w). Uv (MeCN) λ_{max} (lg ε) = 203 (4.49), 217 (4.33, sh), 271 (4.29). *Anal.* Calcd for $C_{12}H_{17}N_5O_3ClPS$: C, 38.15; H, 4.54; N, 18.54; Cl, 9.38; P, 8.20; S, 8.49. Found: C, 38.32; H, 4.44; N, 18.49; Cl, 9.44; P, 8.20; S, 8.47.

Diisopropyl (5-amino-3-methylsulfanyl-1*H*-pyrazol-4-yl)phosphonate (**5.2a**)

Diisopropyl (1-cyano-2,2-bismethylsulfanylvinyl)phosphonate (**2.2**) (1.55 g, 5.00 mmol) and 100 % hydrazine hydrate (**4a**) (250 mg, 5.00 mmol) were stirred in ethanol (5 ml) at room temperature for 1.5 h. The solvent was removed under reduced pressure and the resulting oil treated with ether / pentane (1:2). Compound (**5.2a**) crystallized after storage at -30 °C, *ca.* 12 h. 1.34 g (91 %) **5.2a**, colorless crystals, mp 71 - 72 °C. ^{1}H-Nmr (299.95 MHz, acetone-d_6) δ = 1.23, 1.32 (2 •d, $^3J_{HH}$ = 6.2 Hz, 12H, $OCH(C\underline{H}_3)_2$), 2.43 (s, 3H, SCH_3), 4.51 (dseptet, $^3J_{HH}$ = 6.2 Hz, $^3J_{PH}$ = 8.3 Hz, 2H, $OC\underline{H}(CH_3)_2$), 5.65 (br s, 2H, NH_2). ^{13}C-Nmr (75.43 MHz, acetone-d_6, {^{1}H}) δ = 13.7 (s, SCH_3), [24.1 (d, $^3J_{PC}$ = 5 Hz), 24.3 (d, $^3J_{PC}$ = 4 Hz); $OCH(\underline{C}H_3)_2$], 70.3 (d, $^2J_{PC}$ = 5 Hz, $O\underline{C}H(CH_3)_2$), 85.5 (d, $^1J_{PC}$ = 223 Hz, C-4), 148.6 (d, $^2J_{PC}$ = 12 Hz, C-3), 156.6 (d, $^2J_{PC}$ = 21 Hz, C-5). ^{31}P-Nmr (121.42 MHz, acetone-d_6) δ = 14.3 (s). Ir (KBr, tablet) ν = 3470 (m),

3370 (w), 3340 (w), 3190 (m), 3110 (m), 2980 (m), 2930 (m), 2870 (w), 1630 (m), 1570 (w), 1505 (m), 1385 (w), 1375 (w), 1315 (m), 1310 (m), 1210 (m), 1190 (m), 1170 (m), 1140 (w), 1110 (w), 1100 (m), 990 (s), 970 (s), 935 (w), 885 (w), 785 (w), 775 (w), 740 (w), 620 (w), 610 (m), 535 (w). Uv (MeCN) λ_{max} (lg ε) = 201 (4.23, sh), 266 (3.30, sh). *Anal.* Calcd for $C_{10}H_{20}N_3O_3PS$: C, 40.95; H, 6.87; N, 14.33; P, 10.56; S, 10.93. Found: C, 40.93; H, 6.90; N, 14.32; P, 10.55; S, 10.87.

Diisopropyl (5-amino-3-methylsulfanyl-1-phenyl-1*H*-pyrazol-4-yl)phosphonate (**5.2b**)

Compound (**2.2**) (1.55 g, 5.00 mmol) and phenylhydrazine (**4b**) (541 mg, 5.00 mmol) were stirred in ethanol (5 ml) at room temperature for 1.5 h. After the evaporation of the solvent under reduced pressure, the resulting oil was chromatographed on silica gel (ethyl acetate / hexane (1:1)). 1.39 g (75 %) **5.2b**, colorless oil. ^{1}H-Nmr (299.95 MHz, $CDCl_3$) δ = 1.33, 1.40 (2 • d, $^3J_{HH}$ = 6.2 Hz, 12H, OCH($C\underline{H}_3$)$_2$), 2.54 (s, 3H, SCH_3), 4.62 (dseptet, $^3J_{HH}$ = 6.2 Hz, $^3J_{PH}$ = 8.2 Hz, 2H, O$C\underline{H}$(CH_3)$_2$), 5.29 (br s, 2H, NH_2), 7.35 - 7.57 (m, 5H, H_{ar}). ^{13}C-Nmr (75.43 MHz, $CDCl_3$, {^{1}H}) δ = 13.6 (s, SCH_3), 23.6 - 24.3 (m, OCH($\underline{C}H_3$)$_2$), 70.7 (d, $^2J_{PC}$ = 5 Hz, O$\underline{C}$H(CH_3)$_2$), 86.2 (d, $^1J_{PC}$ = 223 Hz, C-4), 123.5, 127.4, 129.4 (3 • s, C-2' - C-6'), 137.7 (s, C-1'), 149.9 (d, $^2J_{PC}$ = 10 Hz, C-3), 152.7 (d, $^2J_{PC}$ = 24 Hz, C-5). ^{31}P-Nmr (121.42 MHz, $CDCl_3$) δ = 12.8 (s). Ir (NaCl, film) ν = 3400 (m), 3310 (m), 3200 (m), 3060 (w), 3050 (w), 2980 (s), 2930 (m), 2870 (w), 1740 (w), 1600 (s), 1510 (s), 1465 (m), 1455 (s), 1435 (m), 1415 (w), 1385 (s), 1375 (s), 1355 (s), 1315 (m), 1285 (m), 1215 (s), 1175 (s), 1140 (m), 1105 (s), 1075 (m), 1030 (s), 990 (s), 935 (m), 915 (w), 895 (m), 885 (m), 775 (s), 765 (s), 720 (m), 695 (s), 645 (m), 605 (s). Uv (MeCN) λ_{max} (lg ε) = 219 (4.27), 264 (4.03). Exact mass calcd for $C_{16}H_{24}N_3O_3PS$: 369.1276. Found: 369.1277.

General procedure for the preparation of pyrazolo[1,5-*a*]pyrimidines (**7**)

A mixture of dialkyl (5-amino-3-methylsulfanyl-1*H*-pyrazol-4-yl)phosphonate (**5a**) (1.00 mmol) and the corresponding 1,3-diketone (**6**) (5.00 mmol) was refluxed in anhydrous toluene (5 ml) for 3 - 10 h. The solvent was removed under reduced pressure and the resulting semicrystalline residue either washed with ether or chromatographed on silica gel.

Diethyl (5,7-dimethyl-2-methylsulfanylpyrazolo[1,5-*a*]pyrimidin-3-yl)phosphonate (**7.1m**)

Compound (**5.1a**) (266 mg, 1.00 mmol) was treated with pentane-2,4-dione (**6m**) (501 mg, 5.00 mmol). The crude product was digested with ether. 324 mg (98 %) **7.1m**, colorless crystals, mp 118 °C. ^{1}H-Nmr (299.95 MHz, $CDCl_3$) δ = 1.36 (dt, $^3J_{HH}$ = 7.1 Hz, $^4J_{PH}$ = 0.7 Hz, 6H, $OCH_2C\underline{H}_3$), [2.59 (s, 3H), 2.71 (d, J_{PH} = 0.7 Hz, 3H); C-5 – CH_3, C-7 – CH_3], 2.63 (s, 3H, SCH_3), 4.14 - 4.24 (m, 4H, $OC\underline{H}_2CH_3$), 6.60 (d, $^6J_{PH}$ = 0.7 Hz, 1H, H-6). ^{13}C-Nmr (62.89 MHz, $CDCl_3$, {^{1}H}) δ = 13.6 (s, SCH_3), 16.3 (d, $^3J_{PC}$ = 7 Hz, $OCH_2\underline{C}H_3$), 17.0 (s, C-7 – $\underline{C}H_3$), 25.0 (s, C-5 – $\underline{C}H_3$), 62.1 (d, $^2J_{PC}$ = 5 Hz, $O\underline{C}H_2CH_3$), 92.5 (d, $^1J_{PC}$ = 223 Hz, C-3), 109.0 (s, C-6), 145.1 (s, C-7), 151.8 (d, $^2J_{PC}$ = 20 Hz, C-3a), 159.2 (d, $^2J_{PC}$ = 13 Hz, C-2), 161.4 (s, C-5). ^{31}P-Nmr (121.42 MHz, $CDCl_3$) δ = 12.7 (s). Ir (KBr, *tablet*) ν = 2980 (w), 2930 (w), 2900 (w), 1615 (m), 1575 (w), 1560 (m), 1550 (m), 1505 (w), 1445 (w), 1400 (m), 1380 (m), 1370 (w), 1335 (m), 1315 (m), 1280 (w), 1240 (s), 1215 (w), 1165 (w), 1150 (w), 1105 (w), 1055 (m), 1025 (s), 960 (s), 825 (w), 810 (m), 780 (m), 745 (w), 645 (w), 585 (m), 520 (w). Uv (MeCN) λ_{max} (lg ε) = 205 (4.40), 249 (4.58), 304 (3.74). *Anal.* Calcd for $C_{13}H_{20}N_3O_3PS$: C, 47.41; H, 6.12; N, 12.76; P, 9.40; S, 9.74. *Found*: C, 47.40; H, 6.01; N, 12.65; P, 9.39; S, 9.79.

Diethyl (5,6,7-trimethyl-2-methylsulfanylpyrazolo[1,5-*a*]pyrimidin-3-yl)phosphonate (**7.1n**)

Compound (**5.1a**) (266 mg, 1.00 mmol) was treated with 3-methylpentane-2,4-dione (**6n**) (571 mg, 5.00 mmol). The crude product was digested with ether. 330 mg (96 %) **7.1n**, colorless crystals, mp 144 °C. ^{1}H-Nmr (250.13 MHz, $CDCl_3$) δ = 1.35 (t, $^3J_{HH}$ = 7.1 Hz, 6H, $OCH_2C\underline{H}_3$), 2.28 (s, 3H, C-6 – CH_3), 2.58, 2.74 (2 *•s, 2 * 3H, C-5 – CH_3, C-7 – CH_3), 2.63 (s, 3H, SCH_3), 4.09 - 4.27 (m, 4H, $OC\underline{H}_2CH_3$). ^{13}C-Nmr (62.89 MHz, $CDCl_3$, {^{1}H}) δ = 13.6, 13.7, 13.9 (3 * s, SCH_3, C-6 – $\underline{C}H_3$, C-7 – $\underline{C}H_3$), 16.3 (d, $^3J_{PC}$ = 7 Hz, $OCH_2\underline{C}H_3$), 24.4 (s, C-5 – $\underline{C}H_3$), 62.0 (d, $^2J_{PC}$ = 5 Hz, $O\underline{C}H_2CH_3$), 91.9 (d, $^1J_{PC}$ = 224 Hz, C-3), 115.2 (s, C-6), 142.4 (s, C-7), 149.9 (d, $^2J_{PC}$ = 20 Hz, C-3a), 158.1 (d, $^2J_{PC}$ = 12 Hz, C-2), 161.2 (s, C-5). ^{31}P-Nmr (121.42 MHz, $CDCl_3$) δ = 12.9 (s). Ir (KBr, tablet) ν = 2980 (w), 2920 (w), 1610 (m), 1520 (m), 1445 (w), 1420 (w), 1400 (m), 1390 (w), 1380 (w), 1340 (m), 1310 (m), 1270 (m), 1240 (m), 1170 (w), 1105 (w), 1060 (m), 1030 (s), 960 (s), 810 (w), 790 (w), 775 (w), 760 (w), 750 (w), 640 (m), 585 (m),

525 (w). Uv (MeCN) λ_{max} (lg ε) = 209 (4.37), 251 (4.60), 304 (3.72). *Anal.* Calcd for $C_{14}H_{22}N_3O_3PS$: C, 48.97; H, 6.46; N, 12.24; P, 9.02; S, 9.34. Found: C, 48.96; H, 6.30; N, 12.19; P, 9.05; S, 9.58.

Diethyl (2-methylsulfanyl-5,7-diphenylpyrazolo[1,5-*a*]pyrimidin-3-yl)phosphonate (**7.1o**)

Compound (**5.1a**) (266 mg, 1.00 mmol) was treated with 1,3-diphenylpropane-1,3-dione (**6o**) (1.12 g, 5.00 mmol). The crude product was purified by chromatography on silica gel (ethyl acetate / hexane (1:1)). 309 mg (68 %) **7.1o**, colorless crystals, mp 152 °C. ^{1}H-Nmr (299.95 MHz, $CDCl_3$) δ = 1.40 (t, $^3J_{HH}$ = 7.1 Hz, 6H, $OCH_2C\underline{H}_3$), 2.59 (s, 3H, SCH_3), 4.22 - 4.32 (m, 4H, $OC\underline{H}_2CH_3$), 7.44 (s, 1H, H-6), 7.50 - 8.23 (m, 10H, H_{ar}). ^{13}C-Nmr (75.43 MHz, $CDCl_3$, {^{1}H}) δ = 13.6 (s, SCH_3), 16.4 (d, $^3J_{PC}$ = 7 Hz, $OCH_2\underline{C}H_3$), 62.2 (d, $^2J_{PC}$ = 5 Hz, $O\underline{C}H_2CH_3$), 93.5 (d, $^1J_{PC}$ = 223 Hz, C-3), 104.8 (s, C-6), 127.3, 128.4, 128.7, 129.3, 130.7, 131.1 (6 •s, C-2' - C-6', C-2" - C-6"), 136.6 (s, C-1' / C-1"), 146.0 (s, C-7), 152.5 (d, $^2J_{PC}$ = 20 Hz, C-3a), 157.6 (s, C-5), 160.3 (d, $^2J_{PC}$ = 13 Hz, C-2). ^{31}P-Nmr (121.42 MHz, $CDCl_3$) δ = 12.3 (s). Ir (KBr, tablet) ν = 2980 (w), 2930 (w), 2900 (w), 1605 (m), 1575 (m), 1545 (m), 1490 (m), 1450 (w), 1440 (w), 1390 (m), 1375 (m), 1345 (m), 1315 (m), 1280 (w), 1245 (s), 1215 (w), 1165 (m), 1060 (m), 1050 (m), 1020 (s), 965 (m), 950 (m), 850 (w), 770 (m), 755 (m), 735 (w), 700 (w), 690 (m), 585 (m), 560 (w). Uv (MeCN) λ_{max} (lg ε) = 201 (4.62), 272 (4.71), 344 (4.16). *Anal.* Calcd for $C_{23}H_{24}N_3O_3PS$: C, 60.92; H, 5.33; N, 9.27; P, 6.83; S, 7.07. Found: C, 60.98; H, 5.22; N, 9.21; P, 6.75; S, 7.05.

Diisopropyl (5,7-dimethyl-2-methylsulfanylpyrazolo[1,5-*a*]pyrimidin-3-yl)phosphonate (**7.2m**)

Compound (**5.2a**) (294 mg, 1.00 mmol) was treated with pentane-2,4-dione (**6m**) (501 mg, 5.00 mmol). The crude product was digested with ether. 305 mg (85 %) **7.2m**, colorless crystals, mp 124 °C. ^{1}H-Nmr (299.95 MHz, $CDCl_3$) δ = 1.27, 1.40 (2 •d, $^3J_{HH}$ = 6.2 Hz, 12H, $OCH(C\underline{H}_3)_2$), [2.58 (s, 3H), 2.70 (d, J_{PH} = 0.6 Hz, 3H); C-5 – CH_3, C-7 – CH_3], 2.62 (s, 3H, SCH_3), 4.75 (dseptet, $^3J_{HH}$ = 6.2 Hz, $^3J_{PH}$ = 8.3 Hz, 2H, $OC\underline{H}(CH_3)_2$), 6.59 (d, $^6J_{PH}$ = 0.8 Hz, 1H, H-6). ^{13}C-Nmr (75.43 MHz, $CDCl_3$, {^{1}H}) δ = 13.5 (s, SCH_3), 17.0 (s, C-7 – $\underline{C}H_3$), [22.9 (d, $^3J_{PC}$ = 6 Hz), 24.2 (d,

$^3J_{PC}$ = 4 Hz); OCH($\underline{C}H_3)_2$], 24.8 (s, C-5 – $\underline{C}H_3$), 70.6 (d, $^2J_{PC}$ = 5 Hz, O$\underline{C}$H($CH_3)_2$), 93.7 (d, $^1J_{PC}$ = 224 Hz, C-3), 108.7 (s, C-6), 144.7 (s, C-7), 151.2 (d, $^2J_{PC}$ = 20 Hz, C-3a), 159.0 (d, $^2J_{PC}$ = 13 Hz, C-2), 160.7 (s, C-5). ^{31}P-Nmr (121.42 MHz, $CDCl_3$) δ = 10.6 (s). Ir (KBr, tablet) ν = 3050 (w), 2970 (m), 2930 (w), 1615 (m), 1575 (w), 1550 (m), 1505 (w), 1450 (m), 1405 (m), 1385 (w), 1370 (w), 1335 (m), 1320 (m), 1280 (w), 1240 (s), 1180 (w), 1155 (w), 1140 (w), 1110 (w), 1045 (m), 985 (s), 935 (w), 900 (w), 885 (w), 770 (m), 755 (w), 645 (w), 585 (m), 560 (w), 535 (w). Uv (MeCN) λ_{max} (lg ε) = 203 (4.38), 249 (4.58), 303 (3.72). *Anal.* Calcd for $C_{15}H_{24}N_3O_3PS$: C, 50.41; H, 6.77; N, 11.76; P, 8.67; S, 8.97. Found: C, 50.54; H, 6.69; N, 11.67; P, 8.62; S, 8.70.

Diisopropyl (5,6,7-trimethyl-2-methylsulfanylpyrazolo[1,5-*a*]pyrimidin-3-yl)phosphonate (**7.2n**)

Compound (**5.2a**) (294 mg, 1.00 mmol) was treated with 3-methylpentane-2,4-dione (**6n**) (571 mg, 5.00 mmol). The crude product was digested with ether. 341 mg (92 %) **7.2n**, colorless crystals, mp 155 °C. ^{1}H-Nmr (299.95 MHz, $CDCl_3$) δ = 1.27, 1.39 (2 * d, $^3J_{HH}$ = 6.3 Hz, 12H, OCH($\underline{C}H_3)_2$), 2.28 (s, 3H, C-6 – CH_3), 2.57, 2.74 (2 * s, 2 * 3H, C-5 – CH_3, C-7 – CH_3), 2.62 (s, 3H, SCH_3), 4.74 (dseptet, $^3J_{HH}$ = 6.3 Hz, $^3J_{PH}$ = 8.2 Hz, 2H, OC$\underline{H}$($CH_3)_2$). ^{13}C-Nmr (75.43 MHz, $CDCl_3$, {^{1}H}) δ = 13.6, 13.7, 13.9 (3 * s, SCH_3, C-6 – $\underline{C}H_3$, C-7 – $\underline{C}H_3$), 23.9 (d, $^3J_{PC}$ = 5 Hz, OCH($\underline{C}H_3)_2$), 24.3 (s, C-5 – $\underline{C}H_3$), 70.6 (d, $^2J_{PC}$ = 5 Hz, O$\underline{C}$H($CH_3)_2$), 93.4 (d, $^1J_{PC}$ = 224 Hz, C-3), 115.0 (s, C-6), 142.3 (s, C-7), 149.7 (d, $^2J_{PC}$ = 21 Hz, C-3a), 158.2 (d, $^2J_{PC}$ = 13 Hz, C-2), 160.8 (s, C-5). ^{31}P-Nmr (121.42 MHz, $CDCl_3$) δ = 10.3 (s). Ir (KBr, tablet) ν = 2980 (w), 2920 (w), 1610 (m), 1530 (m), 1515 (m), 1470 (w), 1450 (w), 1390 (m), 1370 (m), 1335 (m), 1315 (m), 1270 (m), 1250 (s), 1180 (w), 1145 (w), 1115 (w), 1105 (w), 1040 (m), 990 (s), 980 (m), 895 (w), 885 (w), 875 (w), 775 (w), 765 (w), 745 (m), 555 (m), 545 (w), 530 (w). Uv (MeCN) λ_{max} (lg ε) = 207 (4.37), 250 (4.62), 304 (3.72). *Anal.* Calcd for $C_{16}H_{26}N_3O_3PS$: C, 51.74; H, 7.06; N, 11.31; P, 8.34; S, 8.63. Found: C, 51.58; H, 7.14; N, 11.21; P, 8.25; S, 8.89.

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Dedicated on 80th birthday of Hans Suschitzky, Scientist Emeritus, Salford/Great Britain.

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