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Synthesis of 3-Carbonyl Pyrazole-5-Phosphonates via 1,3-Dipolar Cycloaddition of Bestman-Ohira Reagent with Ynones

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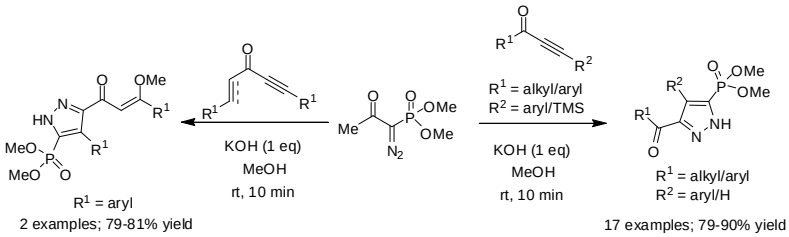
Abstract



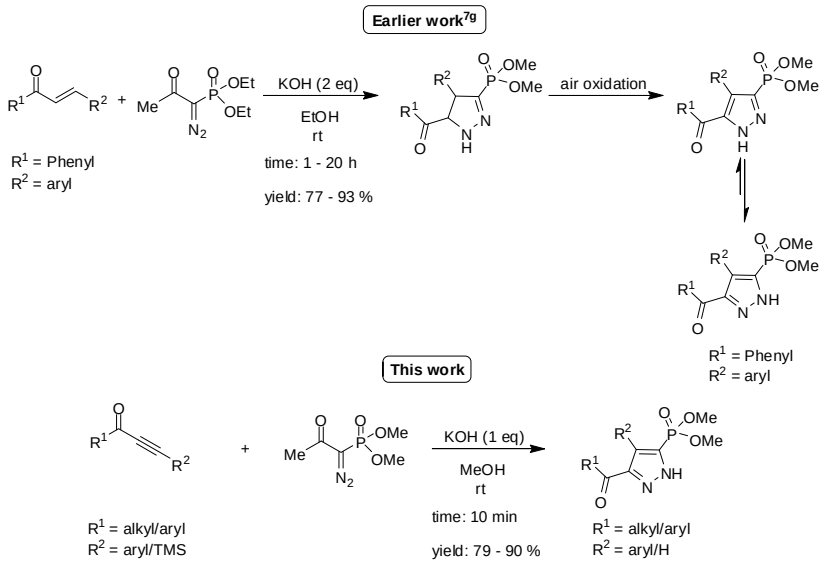
The present work explores the hitherto unexplored reactivity of ynones as dipolarophiles with Bestman Ohira reagent. The reaction offers a convenient route for the synthesis of regioisomerically pure 3,5-disubstituted or 3,4,5-trisubstituted pyrazoles in excellent yields. However, di-ynones and molecules possessing both ynone and enone functionalities provide only monocycloaddition products, whereas another multiple bond undergoes Michael addition with the methoxide anion.

Keywords: Bestmann–Ohira reagent; Dipolar cycloaddition; Ynones; Phosphonyl pyrazole

Introduction

The diazo compounds have been known since more than a century but yet have limited use in industry due to their explosive and toxic nature.[1] However, due to their immense synthetic potential several diazo compounds and methods for their generation have been developed.[2] One such diazo compound is dimethyl (diazomethyl) phosphonate, commonly known as the Seyferth-Gilbert reagent, which upon deprotonation under basic conditions gives dimethyl (diazomethyl) phosphonate anion.[3,4] The dimethyl (diazomethyl) phosphonate anion can also be generated *in situ* by basic methanol promoted deacylation of dimethyl 1-diazo-2-oxopropylphosphonate, commonly known as Bestmann Ohira reagent (BOR).[5]

BOR is commonly used for the conversion of aldehydes into alkynes under mild basic conditions known as Seyferth-Gilbert Homologation,[6] or as the dipole component in the 1,3-dipolar cycloaddition reaction with various dipolarophiles for the synthesis of phosphonylated heterocycles.[7,8] However, to the best of our knowledge, systems with triple bonds have not been investigated for their reactivity as dipolarophiles with BOR in 1,3-dipolar cycloaddition reaction, except for one example of the copper iodide catalyzed reaction of nonactivated alkynes with BOR.[9] The present work explores the reactivity of ynones as dipolarophiles in 1,3-dipolar cycloaddition with BOR. The reaction offers the advantage of introducing various ketoalkyl or ketoaryl or ketoheteroaryl groups at C-3 position and H or alkyl or aryl group at C-4 position of the phosphonyl pyrazole products (Scheme 1).

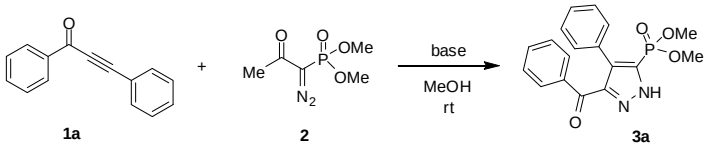


Scheme 1. A schematic representation of the present work *vs* earlier work

Results and Discussion

The reaction conditions were optimized with 1,3-diphenylprop-2-yn-1-one **1a** as the model substrate. Various bases reported suitable for the effective generation of the dimethyl (diazomethyl) phosphonate anion were employed (Table 1). The product **3a** was obtained in comparable yields in case of NaOMe, KO^{t}Bu and K_2CO_3, however reaction took longer time to complete in later two cases (Table 1, entries 2-3). The reaction was complete in 10 minutes when KOH was employed affording product **3a** in excellent yield (table 1, entry 4). When 1 equivalent of KOH was used instead of 2 equivalents, a marginal reduction in yield was noticed (Table 1, entry 5) however, taking into account the economy of the reaction, the 1 equivalent of KOH in MeOH was selected as the optimized condition.

Table 1. Optimization of Conditions for the Reaction of Ynone **1a** with BOR **2**[a]

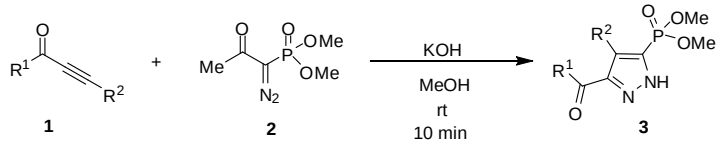


Entry	Base[b]	Time (min)	Yield of 3a (%)[c]
1	NaOMe	20	60
2	KO^{t}Bu	120	65
3	K_2CO_3	180	70
4	KOH	10	81
5	KOH[d]	10	79

[a] All reactions were performed with 1 mmol of **1a** with 1.2 mmol of **2** in 5 mL of solvent; [b] 2.4 mmol (2 equiv) of base was employed; [c] Yields of product isolated after column chromatography; [d] 1.2 mmol (1 equiv) of KOH was employed.

The optimized conditions were employed for the reaction of BOR with several other ynones including TMS-alkynones, which were selected to prepare 3,5-disubstituted pyrazoles as TMS group may undergo deprotection under the reaction conditions (Table 2).[10]

Table 2. Reaction of Ynones **1** with BOR **2** under Optimized Conditions[a]



1 2 3

Entry	1/3	R^1	R^2	Yield of 3 (%)[b]
1	**a**	Ph	Ph	79
2	**b**	Ph	4-Me-Ph	89
3	**c**	Ph	4-F-Ph	89
4	**d**	3-OMe-Ph	Ph	87
5	**e**	3-OMe-Ph	4-Me-Ph	88
6	**f**	3-OMe-Ph	4-F-Ph	79
7	**g**	2-Furyl	Ph	87
8	**h**	2-Furyl	4-Me-Ph	85
9	**i**	cyclohexyl	Ph	88
10	**j**	cyclohexyl	4-Me-Ph	85
11	**k**	cyclohexyl	4-F-Ph	90
12	**l**	isopropyl	Ph	85
13	**m**	isobutyl	Ph	88
14	**n**	*n*-pentyl	Ph	88
15	**o**	Ph	TMS (H in **3**)	87
16	**p**	3-OMe-Ph	TMS (H in **3**)	86
17	**q**	2-Furyl	TMS (H in **3**)	84

[a] All reactions were performed at 1 mmol scale of **1** with 1.2 mmol of **2** and 1.2 mmol of KOH in 5 mL of MeOH; [b] Yields of product isolated after column chromatography

It is noteworthy that the substrate scope of the reaction is appreciable as is evident from the variety of ynones utilized. The ynones with aryl (Table 2, entries 1-6, 15, 16) or heteroaryl (Table 2, entries 7, 8, 17) or alkyl group (Table 2, entries 9-14) in the carbonyl part provided the carbonyl phosphonylpyrazoles in excellent yields. Similarly, the aryne part of the ynones utilized, bears phenyl ring with both electron donating (Table 2, entries 2, 5, 8, 10) as well as electron withdrawing substituents (Table 2, entries 3, 6, 11) and also TMS group which undergoes hydrolysis during the reaction to provide trisubstituted phosphonylpyrazoles (Table 2, entries 15 - 17).

The proposed mechanism for the reaction involves *in situ* generation of the dimethyl (diazomethyl) phosphonate anion **A** by basic methanol promoted deacylation of the Bestmann Ohira reagent **2**. Anion **A** undergoes formal intramolecular 1,3-dipolar cycloaddition with **1** leading to the intermediate **C** via the allenic anion **B**. The intermediate **C** after intramolecular proton migration leads to the corresponding carbonyl phosphonylpyrazole **3** (Figure 1).[7f,g]

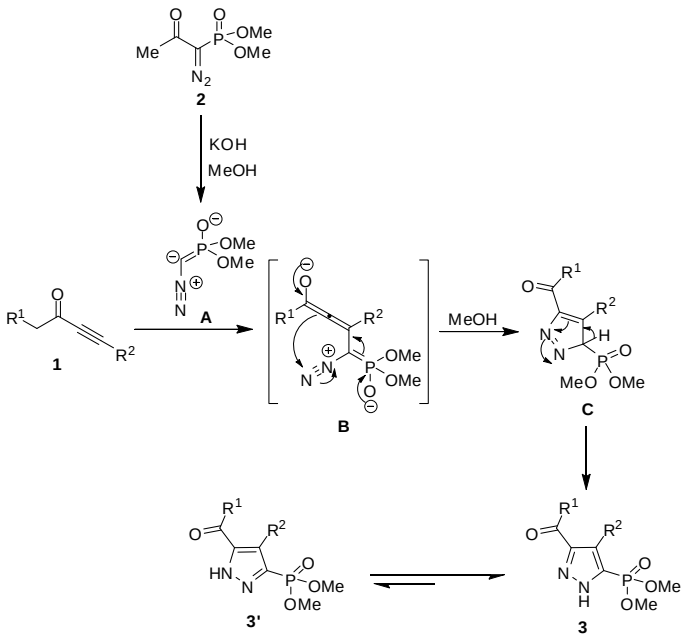


Figure 1. Proposed reaction mechanism

Among the two tautomers **3** and **3'**, the more stable **3** is the exclusive tautomer in solid state as well as in the solution as is evident by the crystal structure (Figure 2) and NMR (^{1}H & ^{31}P) analysis.[7g, 11]

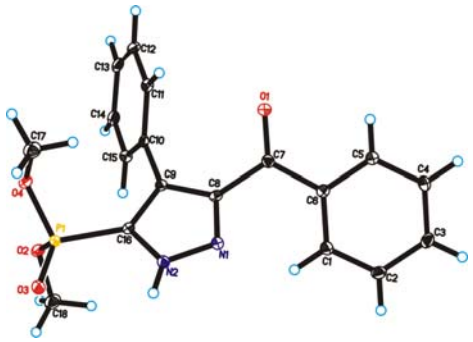
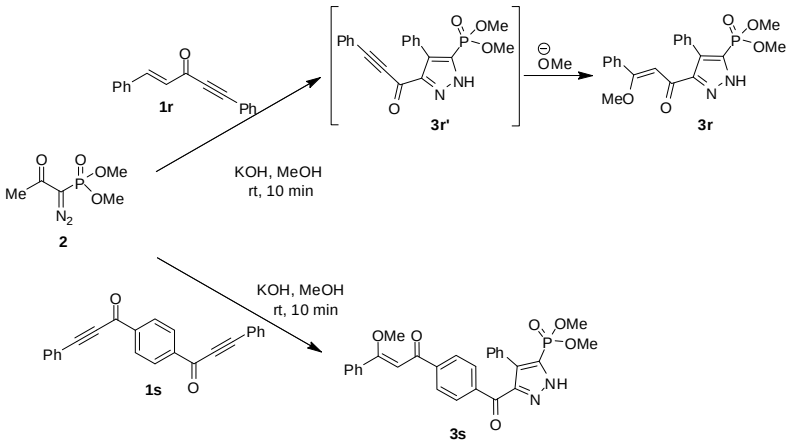


Figure 2. ORTEP diagram of **3a**

At this step, in order to study the relative reactivity of enones and ynones, we prepared the ene-ynone **1r** and subjected that to the 1,3-dipolar cycloaddition with BOR under optimized conditions (Table 3, entry 1). The product **3r** shows that the cycloaddition takes place at the double bond whereas the triple bond undergoes Michael addition with the methoxide anion. It can be predicted that first cycloaddition takes place resulting into the formation of **3r'** which then instead of second cycloaddition undergoes Michael addition with the methoxide anion due to steric factors. In order to gain more insight into this cycloaddition-Michael addition mechanism, we selected the *bis*-ynone **1s**, synthesized from terephthalic acid, as the substrate with two equivalent triple bonds devoid of any mutual steric constraint. However, in this case also only monocycloaddition product **3s** could be obtained with another triple bond undergoing Michael addition with the methoxide anion (Table 3, entry 2).

Table 3. Reaction of ynones **1r** and **1s** with BOR **2** under Optimized Conditions[a]



Entry	1/3	Yield of 3 (%)[b]
1	**r**	79
2	**s**	89

[a]All reactions were performed at 1 mmol scale of **1** with 2.4 mmol of **2** and 2.4 mmol of KOH in 10 mL of MeOH; [b] Yields of product isolated after column chromatography.

Conclusion

In conclusion, ynones **1a-q** were subjected to 1,3-dipolar cycloaddition reaction with BOR **2** for the construction of pyrazole phosphonates **3a-q** in excellent yields. The pyrazole-5-phosphonate was found to be the exclusive tautomer in solid (X-ray) as well as in solution state (NMR). Similar reaction of BOR with molecules containing two dipolarophilic sites such as **1r, s** afforded monocycloaddition products **3r** and **3s**, respectively whereas another site prefers Michael addition with the methoxide anion.

Experimental

All reactions were monitored by TLC, visualization was effected with UV and/or by developing in iodine. Chromatography refers to open column chromatography on silica gel (Merck, 100-200 mesh). Melting points recorded are uncorrected. IR spectra were recorded on a Perkin Elmer's RX I FTIR spectrophotometer. NMR spectra were recorded on a Brucker Avance spectrometer and chemical shifts are reported in δ (ppm) relative to TMS as the internal standard for ^{1}H and ^{13}C and phosphoric acid as the external standard for ^{31}P. To describe spin multiplicity, standard abbreviations such as s, d, t, q, m, dd referring to singlet, doublet, triplet, quartet, multiplet and doublet of doublet respectively, are used. The coupling constants (*J*) are given in Hz. The ESI-LRMS were recorded on Thermo Finnigan LCQ Advantage-Ion Trap Mass spectrometer and the ESI-HRMS spectra were recorded on Agilent 6520- Q-TofLC/MS system.

All reactions were conducted in oven-dried glasswares under nitrogen. Methanol was distilled over sodium and benzophenone. Dimethyl oxopropyl phosphonate was purchased from Sigma Aldrich and used as received for the synthesis of the Bestmann-Ohira reagent 2.[5a, b] All other reagents were purchased from local suppliers and used without purification. Ynones were prepared following standard Sonogashira coupling protocol as detailed below. The spectroscopic details for the unreported alkynones and appropriate citations for the reported alkynones are provided.

General procedure for the preparation of ynones 1 from acetyl chlorides

To a round bottom flask were added CuI (0.05 mmol), $PdCl_2(PPh_3)_2$ (0.01 mmol) and triethylamine (5 mL). The flask was flushed with nitrogen and the terminal acetylene (2.5 mmol) was added to the stirred suspension, followed by dropwise addition of acid chloride (3.25 mmol, 1.3 equiv). The resulting mixture was allowed to stir at room temperature until

completion of reaction (monitored by TLC), filtered through a plug of silica gel, and concentrated under reduced pressure. The residue was then purified by column chromatography on silica gel to afford the desired ynone **1**.

1,3-Diphenylprop-2-yn-1-one (1a)[12]

Purification by flash chromatography (95/5 hexane/EtOAc) afforded 83% (171 mg) of the product with spectral properties identical to those previously reported.

1-Phenyl-3-p-tolylprop-2-yn-1-one (1b)[13]

Purification by flash chromatography (95/5 hexane/EtOAc) afforded 81% (178 mg) of the product with spectral properties identical to those previously reported.

3-(4-Fluorophenyl)-1-phenylprop-2-yn-1-one (1c)[14]

Purification by flash chromatography (95/5 hexane/EtOAc) afforded 72% (161 mg) of the product with spectral properties identical to those previously reported.

1-(3-Methoxyphenyl)-3-phenylprop-2-yn-1-one (1d)[12]

Purification by flash chromatography (95/5 hexane/EtOAc) afforded 78% (184 mg) of the product with spectral properties identical to those previously reported.

1-(3-Methoxyphenyl)-3-p-tolylprop-2-yn-1-one (1e)

Purification by flash chromatography (95/5 hexane/EtOAc) afforded 72% (180 mg) of the product.

Colorless solid; R_f 0.50 (20% EtOAc/hexane); Mp 78-80 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.77-7.79 (m, 1H), 7.63 (q, J = 4.0 Hz, 1H), 7.51 (d, J = 8.1 Hz, 2H), 7.35 (t, J = 8.1 Hz, 1H), 7.15 (d, J = 8.4 Hz, 2H), 7.09-7.11 (m, 1H), 3.81 (s, 3H), 2.33 (s, 3H); ^{13}C NMR ($CDCl_3$) δ: 177.8 (CO), 159.8 (C_{Ar}), 141.6 (C_{Ar}), 138.4 (C_{Ar}), 133.1 ($C_{Ar}H$ x 2), 129.6 ($C_{Ar}H$), 129.5 ($C_{Ar}H$ x 2), 122.8 ($C_{Ar}H$), 120.8 ($C_{Ar}H$), 117.0 (C_{Ar}), 112.9 ($C_{Ar}H$), 93.7 (C≡C), 86.9 (C≡C), 55.5 (OCH_3), 21.8 (CH_3).

3-(4-Fluorophenyl)-1-(3-methoxyphenyl)prop-2-yn-1-one (1f)

Purification by flash chromatography (95/5 hexane/EtOAc) afforded 68% (173 mg) of the product.

Colorless solid; R_f 0.50 (20% EtOAc/hexane); Mp 82-84 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, J = 7.8 Hz, 1H), 7.62 (br t, 2H merged with s, 1H, J = 8.5 Hz, 5.4 Hz), 7.36 (t, J = 7.8 Hz, 1H), 7.11 (dd, J = 8.2 Hz, 2.0 Hz, 1H), 7.05 (t, J = 8.5 Hz, 2H), 3.82 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.6 (CO), 164.1 (d, $J_{C\text{-}F}$ = 252.3 Hz, C_{Ar}), 159.9 (C_{Ar}), 138.2 (C_{Ar}), 135.4 ($C_{Ar}H$), 135.3 ($C_{Ar}H$), 129.7 ($C_{Ar}H$), 122.8 ($C_{Ar}H$), 120.9 ($C_{Ar}H$), 116.4 ($C_{Ar}H$), 116.3 (d, $J_{C\text{-}F}$ = 3.7 Hz, C_{Ar}), 116.2 ($C_{Ar}H$), 112.9 ($C_{Ar}H$), 91.9 (C≡C), 86.9 (C≡C), 55.5 (OCH_3).

1-(Furan-2-yl)-3-phenylprop-2-yn-1-one (1g)[12]

Purification by flash chromatography (95/5 hexane/EtOAc) afforded 80% (157 mg) of the product with spectral properties identical to those previously reported.

1-(Furan-2-yl)-3-p-tolylprop-2-yn-1-one (1h)[15]

Purification by flash chromatography (95/5 hexane/EtOAc) afforded 82% (172 mg) of the product with spectral properties identical to those previously reported.

*1-Cyclohexyl-3-phenylprop-2-yn-1-one (**1i**)*[12]

Purification by flash chromatography (95/5 hexane/EtOAc) afforded 64% (136 mg) of the product with spectral properties identical to those previously reported.

*1-Cyclohexyl-3-p-tolylprop-2-yn-1-one (**1j**)*[16]

Purification by flash chromatography (95/5 hexane/EtOAc) afforded 60% (136 mg) of the product with spectral properties identical to those previously reported.

*1-Cyclohexyl-3-(4-fluorophenyl)prop-2-yn-1-one (**1k**)*

Purification by flash chromatography (95/5 hexane/EtOAc) afforded 54% (124 mg) of the product.

Brown viscous liquid; R_f 0.50 (20% EtOAc/hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 – 7.50 (t split into m, 2H), 6.96 – 7.00 (t split into m, 2H), 2.37 –2.43 (m, 1H), 1.93 – 1.97 (m,

2H), 1.78 – 1.82 (m, 1H), 1.70 – 1.74 (m, 2H), 1.48 – 1.52 (m, 2H), 1.35 – 1.41 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.3 (CO), 163.9 (d, J_{C-F} = 251.7 Hz, C_{Ar}), 135.3 ($C_{Ar}H$), 135.2 ($C_{Ar}H$), 116.3 (d, J_{C-F} = 3.6 Hz, C_{Ar}), 116.2 ($C_{Ar}H$), 116.0 ($C_{Ar}H$), 90.2 (C≡C), 87.2 (C≡C), 52.3 ($C_{Ali}H$), 28.3 (CH_2 x 2), 25.8 (CH_2), 25.4 (CH_2 x 2).

*4-Methyl-1-phenylpent-1-yn-3-one (**1l**)*[17]

Purification by flash chromatography (95/5 hexane/EtOAc) afforded 66% (114 mg) of the product with spectral properties identical to those previously reported.

*5-Methyl-1-phenylhex-1-yn-3-one (**1m**)*[18]

Purification by flash chromatography (95/5 hexane/EtOAc) afforded 69% (128 mg) of the product with spectral properties identical to those previously reported.

*1-Phenyloct-1-yn-3-one (**1n**)*[19]

Purification by flash chromatography (95/5 hexane/EtOAc) afforded 62% (124 mg) of the product with spectral properties identical to those previously reported.

*1-Phenyl-3-(trimethylsilyl)prop-2-yn-1-one (**1o**)*[20]

Purification by flash chromatography (95/5 hexane/EtOAc) afforded 73% (158 mg) of the product with spectral properties identical to those previously reported.

*1-(3-Methoxyphenyl)-3-(trimethylsilyl)prop-2-yn-1-one (**1p**)*[21]

Purification by flash chromatography (95/5 hexane/EtOAc) afforded 70% (162 mg) of the product with spectral properties identical to those previously reported.

*1-(Furan-2-yl)-3-(trimethylsilyl)prop-2-yn-1-one (**1q**)*[22]

Purification by flash chromatography (95/5 hexane/EtOAc) afforded 74% (152 mg) of the product with spectral properties identical to those previously reported.

*(E)-1,5-Diphenylpent-1-en-4-yn-3-one (**1r**)*[12]

Purification by flash chromatography (95/5 hexane/EtOAc) afforded 80% (186 mg) of the product with spectral properties identical to those previously reported.

*1,1'-(1,4-Phenylene)bis(3-phenylprop-2-yn-1-one) (**1s**)*[12]

Purification by flash chromatography (95/5 hexane/EtOAc) afforded 80% (267 mg) of the product with spectral properties identical to those previously reported.

*General procedure for 1, 3-dipolar cycloaddition between ynones **1** & BOR **2***

To a stirred solution of ynone **1a-q** (1 mmol) and Bestmann-Ohira reagent **2** (1.2 mmol or 2.4 mmol in case of **1r** and **1s**) in dry MeOH (5 mL or 10 mL in case of **1r** and **1s**), was added KOH (1.2 mmol or 2.4 mmol in case of **1r** and **1s**) and the reaction mixture was stirred at room temperature until the completion of the reaction (monitored by TLC). Methanol was distilled off under reduced pressure. The residue was dissolved in ethyl acetate (20 mL) and washed with saturated ammonium chloride (2 x 20 mL). The combined organic layers were washed with brine (2 x 10 mL), dried over anhyd. Na_2SO_4 and concentrated in vacuo. The crude product was purified by column chromatograpy on silica gel (40% EtOAc/hexane) to afford the products **3a-s**.

*Dimethyl 3-Benzoyl-4-phenyl-1H-pyrazol-5-ylphosphonate (**3a**)*

Brown solid; isolated yield 79% (281 mg). R_f 0.30 (70% EtOAc/hexane); Mp 153-155 °C; IR (KBr, cm^{-1}): 3055, 2989, 2358, 1656, 1598, 1450, 1422, 1264, 1035, 733, 701; ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.63 (bs, 1H), 7.93 (d, J = 7.6 Hz, H), 7.50 (m, 1H), 7.30-7.38 (m, 7H), 3.68 (d, J_{H-P} = 11.6 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.3 (CO), 136.9 (C_{Ar} x 2), 132.9 ($C_{Ar}H$), 130.5 (C_{pyr}), 130.3 ($C_{Ar}H$ x 2), 129.9 ($C_{Ar}H$ x 2), 128.0 ($C_{Ar}H$ x 2), 127.9 ($C_{Ar}H$), 127.8 ($C_{Ar}H$ x 2), 53.4 (d, J_{C-P} = 5.1 Hz, {PO}OCH_3 x 2); ^{31}P NMR (161.9 MHz, $CDCl_3$) δ 9.07; MS (ES+) m/e (rel intensity): 357.1 (MH^+, 100), 358.1 (20), 329.1 (11); HRMS for $C_{18}H_{17}N_2O_4P$: calcd. (MH^+): 357.1004, found: 357.0990.

Single crystal X-ray data: Crystal structure of compound **3a** has been deposited at the Cambridge Crystallographic Data Center and allocated the reference no. CCDC 983093.

*Dimethyl 3-benzoyl-4-p-tolyl-1H-pyrazol-5-ylphosphonate (**3b**)*

Brown solid; isolated yield 89% (329 mg). R_f 0.30 (70% EtOAc/hexane); Mp 189-191°C; IR (KBr, cm^{-1}): 3006 (br w), 2363 (w), 1660 (w), 1276 (s), 1261 (s), 1036 (m), 750 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, J = 7.5 Hz, 2H), 7.42 (t, J = 7.2 Hz, 1H), 7.28 (t, J = 7.5 Hz, 2H), 7.16 (d merged with $CDCl_3$ peak, J = 7.8 Hz, 2H), 7.03 (d, J = 7.6 Hz, 2H), 3.60 (d, J_{H-P} = 11.5 Hz, 6H), 2.25 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.2 (CO), 137.7 (C_{Ar}), 136.9 (C_{Ar}), 133.0 (C_{pyr}), 132.9 ($C_{Ar}H$), 130.3 ($C_{Ar}H$ x 2), 129.7 ($C_{Ar}H$ x 2), 128.6 ($C_{Ar}H$ x 2), 128.0 ($C_{Ar}H$ x 2), 127.3 (C_{Ar}), 53.4 ({PO}OCH_3 x 2), 21.2 (CH_3); ^{31}P NMR (161.9 MHz, $CDCl_3$) δ 9.17; MS (ES+) m/e (rel intensity): 371.1 (MH^+, 100), 372.1 (21); HRMS for $C_{19}H_{19}N_2O_4P$: calcd. (MH^+): 371.1161, found: 371.1145.

*Dimethyl 3-benzoyl-4-(4-fluorophenyl)-1H-pyrazol-5-ylphosphonate (**3c**)*

Brown solid; isolated yield 89% (333 mg). R_f 0.30 (70% EtOAc/hexane); Mp 178-180 °C; IR (KBr, cm^{-1}): 3443 (br w), 3110 (br w), 2925 (m), 2853 (w), 1683 (m), 1646 (w), 1433 (m), 1260 (s), 1027 (s), 750 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.80 (bs, 1H), 7.86 (d, J = 7.3 Hz, 2H), 7.44 (t, J = 7.3 Hz, 1H), 7.28 – 7.31 (m, 4H), 6.93 (t, J = 8.4 Hz , 2H), 3.62 (d, J_{H-P} = 11.5 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.2 (CO), 162.5 (d, J_{C-F} = 246.2 Hz, C_{Ar}), 136.9 (C_{Ar}), 133.1 ($C_{Ar}H$), 131.8 ($C_{Ar}H$), 131.7 ($C_{Ar}H$), 130.3 ($C_{Ar}H$ x 2), 129.5 (d, J_{C-P} = 18.4 Hz, C_{pyr}), 128.1 ($C_{Ar}H$ x 2), 126.4 (d, J_{C-F} = 2.6 Hz, C_{Ar}), 114.9 ($C_{Ar}H$), 114.8($C_{Ar}H$), 53.4 (d, J_{C-P} = 5.3 Hz, {PO}OCH_3 x 2); ^{31}P NMR (161.9 MHz, $CDCl_3$) δ: 8.93; MS (ES+) m/e (rel intensity): 375.1 (MH^+, 100), 376.1 (20); HRMS for $C_{18}H_{16}FN_2O_4P$: calcd. (MH^+): 375.0910, found: 375.0895.

*Dimethyl 3-(3-methoxybenzoyl)-4-phenyl-1H-pyrazol-5-ylphosphonate (**3d**)*

Colorless solid; isolated yield 87% (336 mg). R_f 0.30 (70% EtOAc/hexane); Mp 119-120 °C; IR (KBr, cm^{-1}): 3054 (br w), 2989 (w), 2362 (w), 1662 (w), 1264 (s), 1038 (m), 730 (s), 701 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 13.26 (br s, 1H), 7.33 – 7.58 (m, 8H), 7.07 (s, 1H), 3.79 (s, 3H), 3.70 (d, J_{H-P} = 11.4 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.1 (CO), 159.4 (C_{Ar}), 138.2 (C_{Ar}), 130.6 (C_{Ar}), 130.5 (d merged with C_{Ar} at 130.6, J_{C-P} = 13.4 Hz, C_{pyr}), 129.9 ($C_{Ar}H$ x 2), 129.1 ($C_{Ar}H$), 127.9 ($C_{Ar}H$), 127.9 ($C_{Ar}H$ x 2), 123.5 ($C_{Ar}H$), 119.8 ($C_{Ar}H$), 114.3 ($C_{Ar}H$), 55.4 (OCH_3), 53.4 (d, J_{C-P} = 5.0 Hz, {PO}OCH_3 x 2); ^{31}P NMR (161.9 MHz, $CDCl_3$) δ 9.09; MS (ES+) m/e (rel intensity): 387.1 (MH^+, 100), 388.1 (22); HRMS for $C_{19}H_{19}N_2O_5P$: calcd. (MH^+): 387.1110, found: 387.1100.

*Dimethyl 3-(3-methoxybenzoyl)-4-p-tolyl-1H-pyrazol-5-ylphosphonate (**3e**)*

Light Brown solid; isolated yield 88% (352 mg). R_f 0.30 (70% EtOAc/hexane); Mp 122-124 °C; IR (KBr, cm^{-1}): 3119 (br w), 2955 (w), 1659 (m), 1485 (m), 1275 (s), 1031 (s), 765 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.69 (bs, 1H), 7.49 (d, J = 7.3 Hz, 1H), 7.40 (s, 1H), 7.18 (d, J = 7.0 Hz, 2H merged with s, 1H), 7.05 (d, J = 7.8 Hz, 2H), 6.98 (dd collapsed into t, J = 8.0 Hz, 1.6 Hz, 1H), 3.70 (s, 3H), 3.61 (d, J_{H-P} = 11.6 Hz, 6H), 2.26 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.1 (CO), 159.3(C_{Ar}), 138.2 (C_{Ar}), 137.6 (C_{Ar}), 130.6 (d, J_{C-P} = 18.4 Hz, C_{pyr}), 129.7 ($C_{Ar}H$ x 2), 128.9 ($C_{Ar}H$), 128.5 ($C_{Ar}H$ x 2), 127.4 (C_{Ar}), 123.4 ($C_{Ar}H$), 119.7 ($C_{Ar}H$), 114.2 ($C_{Ar}H$), 55.3 (OCH_3), 53.3 (d, J_{C-P} = 4.9 Hz, {PO}OCH_3 x 2), 21.2 (CH_3); ^{31}P NMR (161.9 MHz, $CDCl_3$) δ 9.32; MS (ES+) m/e (rel intensity): 401.1 (MH^+, 100), 402.1 (21); HRMS for $C_{20}H_{21}N_2O_5P$: calcd. (MH^+): 401.1266, found: 401.1253.

*Dimethyl 4-(4-fluorophenyl)-3-(3-methoxybenzoyl)-1H-pyrazol-5-ylphosphonate (**3f**)*

Colorless viscous liquid; isolated yield 79% (319 mg). R_f 0.30 (70% EtOAc/hexane); IR (Film, cm^{-1}): 3053 (br w), 3006 (br w), 2988 (br w), 2360 (w), 1422 (w), 1264 (s), 1037 (w), 731 (s), 702 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (d, J = 7.6 Hz, 1H), 7.39 (br s, 1H), 7.26 – 7.30 (m, 2H), 7.19 (t, J = 3.9 Hz, 1H), 6.98 – 7.00 (m, 1H), 6.94 (t, J = 8.7 Hz, 2H), 3.72 (s, 1H), 3.62 (d, J_{H-P} = 11.5 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.9 (CO), 162.6 (d, J_{C-F} = 246.3 Hz, C_{Ar}), 159.4 (C_{Ar}), 138.1 (C_{Ar}), 131.8 ($C_{Ar}H$), 131.7 ($C_{Ar}H$), 129.5 (d, J_{C-P} = 18.8 Hz, C_{pyr}), 129.1 ($C_{Ar}H$), 126.4 (d, J_{C-F} = 3.2 Hz, C_{Ar}), 123.3 ($C_{Ar}H$), 119.8 ($C_{Ar}H$), 115.0 ($C_{Ar}H$), 114.8 ($C_{Ar}H$), 114.3 ($C_{Ar}H$), 55.4 (OCH_3), 53.4 (d, J_{C-P} = 5.5 Hz, {PO}OCH_3 x 2);

^{31}P NMR (161.9 MHz, $CDCl_3$) δ 8.88; MS (ES+) m/e (rel intensity): 405.0 (MH^+, 100), 406.1 (22); HRMS for $C_{19}H_{18}FN_2O_5P$: calcd. (MH^+): 405.1016, found: 405.1017.

*Dimethyl 3-(furan-2-carbonyl)-4-phenyl-1H-pyrazol-5-ylphosphonate (**3g**)*

Colorless solid; isolated yield 87% (301 mg). R_f 0.30 (70% EtOAc/hexane); Mp 171-172 °C; IR (KBr, cm^{-1}): 3054 (br w), 2988 (w), 2359 (w), 1649 (w), 1470 (w), 1264 (s), 1033 (m), 730 (s), 700 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.94 (bs, 1H), 7.55 (s, 1H), 7.48 (bs, 1H), 7.28 – 7.35 (m, 5H), 6.45 (dd, J = 3.5 Hz, 1.6 Hz, 1H), 3.59 (d, $J_{H\text{-}P}$ = 11.6 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.5 (CO), 151.7 (C_{fur}), 147.5 ($C_{fur}H$), 130.6 (d, $J_{C\text{-}P}$ = 18.7 Hz, C_{pyr}), 130.4 (C_{Ar}), 129.9 ($C_{Ar}H$ x 2), 128.0 ($C_{Ar}H$), 127.8($C_{Ar}H$ x 2), 122.1 ($C_{fur}H$), 112.3 ($C_{fur}H$), 53.4 (d, $J_{C\text{-}P}$ = 5.1 Hz, {PO}OCH_3 x 2); ^{31}P NMR (161.9 MHz, $CDCl_3$) δ 8.69; MS (ES+) m/e (rel intensity): 347.0 (MH^+, 100), 348.0 (19); HRMS for $C_{16}H_{15}N_2O_5P$: calcd. (MH^+): 347.0797, found: 347.0786.

Dimethyl 3-(furan-2-carbonyl)-4-p-tolyl-1H-pyrazol-5-ylphosphonate (**3h**)

Brown solid; isolated yield 85% (306 mg). R_f 0.30 (70% EtOAc/hexane); Mp 199-200 °C; IR (KBr, cm^{-1}): 3054 (br w), 2989 (w), 2360 (w), 1649 (w), 1264 (s), 1038 (m), 730 (s), 702 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (s, 1H), 7.45 (d appearing as bs, 1H), 7.22 (d, J = 7.2 Hz, 2H), 7.10 (d, J = 7.6 Hz, 2H), 6.44 (dd appearing as t, J = 3.2 Hz, 1.5 Hz, 2H), 3.59 (d, $J_{H\text{-}P}$ = 11.6 Hz, 6H), 2.29 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.7 (CO), 151.0 (C_{fur}), 146.6 ($C_{fur}H$), 136.9 (C_{Ar}), 129.9 (d, $J_{C\text{-}P}$ = 18.2 Hz, C_{pyr}), 129.0 ($C_{Ar}H$ x 2), 127.8 ($C_{Ar}H$ x 2), 126.4 (C_{Ar}), 121.2 ($C_{fur}H$), 111.4 ($C_{fur}H$), 52.6 (d, $J_{C\text{-}P}$ = 5.0 Hz, {PO}OCH_3 x 2), 20.5 (CH_3); ^{31}P NMR (161.9 MHz, $CDCl_3$) δ 8.93; MS (ES+) m/e (rel intensity): 361.0 (MH^+, 100), 362.0 (20); HRMS for $C_{17}H_{17}N_2O_5P$: calcd. (MH^+): 361.0953, found: 361.0943.

*Dimethyl 3-(cyclohexanecarbonyl)-4-phenyl-1H-pyrazol-5-ylphosphonate (**3i**)*

Colorless solid; isolated yield 88% (319 mg). R_f 0.30 (70% EtOAc/hexane); Mp 134-136 °C; IR (KBr, cm^{-1}): 3122 (br w), 2930 (m), 2854 (w), 1686 (m), 1449 (m), 1275 (s), 1033 (s), 764 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 – 7.31 (m, 5H), 3.57 (d, $J_{H\text{-}P}$ = 11.5 Hz, 6H), 2.99 (bs, 1H), 1.54 -1.75 (m, 5H), 1.11 – 1.35 (m, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.4 (CO), 130.8 (C_{Ar}), 129.9 ($C_{Ar}H$ x 2), 129.6 (d, $J_{C\text{-}P}$ = 19.0 Hz, C_{pyr}), 128.1 ($C_{Ar}H$), 127.8 ($C_{Ar}H$ x 2), 53.3 (d, $J_{C\text{-}P}$ = 5.4 Hz, {PO}OCH_3 x 2), 47.0 ($CH_{aliphatic}$), 28.7 (CH_2 x 2), 25.8 (CH_2), 25.5 (CH_2 x 2); ^{31}P NMR (161.9 MHz, $CDCl_3$) δ 9.15; MS (ES+) m/e (rel intensity): 363.1 (MH^+, 100), 364.1 (20); HRMS for $C_{18}H_{23}N_2O_4P$: calcd. (MH^+): 363.1474, found: 363.1470.

*Dimethyl 3-(cyclohexanecarbonyl)-4-p-tolyl-1H-pyrazol-5-ylphosphonate (**3j**)*

Colorless solid; isolated yield 85% (320 mg). R_f 0.30 (70% EtOAc/hexane); Mp 194-195 °C; IR (KBr, cm^{-1}): 3005 (br w), 2989 (br w), 2362 (w), 1686 (w), 1429 (w), 1264 (s), 1036 (m), 764 (s), 748 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.13 – 7.17 (m, 4H), 3.57 (d, $J_{H\text{-}P}$ = 11.5 Hz, 6H), 3.03 (bs, 1H), 2.33 (s, 3H), 1.54 -1.74 (m, 5H), 0.81 – 1.31 (m, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.4 (CO), 137.9 (C_{Ar} x 2), 129.7 ($C_{Ar}H$ x 2), 128.5 ($C_{Ar}H$ x 2), 127.6 (C_{pyr}), 53.2 (d, $J_{C\text{-}P}$ = 5.4 Hz, {PO}OCH_3 x 2), 46.9 ($CH_{aliphatic}$), 28.7 (CH_2 x 2), 25.8 (CH_2), 25.5 (CH_2 x 2), 21.3 (CH_3); ^{31}P NMR (161.9 MHz, $CDCl_3$) δ 9.40; MS (ES+) m/e (rel intensity): 377.1 (MH^+, 100), 378.1 (21); HRMS for $C_{19}H_{25}N_2O_4P$: calcd. (MH^+): 377.1630, found: 377.1621.

*Dimethyl 3-(cyclohexanecarbonyl)-4-(4-fluorophenyl)-1H-pyrazol-5-ylphosphonate (**3k**)*

Colorless solid; isolated yield 90% (342 mg). R_f 0.30 (70% EtOAc/hexane); Mp 153-155 °C; IR (KBr, cm^{-1}): 3119 (br w), 2929 (m), 2854 (m), 1685 (m), 1275 (m), 1222 (s), 1027 (s), 953 (s), 837 (s), 702 (s); ^{1}H NMR (400 MHz, $CDCl_3$,) δ 7.27 (dd, J = 5.4 Hz, 2.1 Hz, 2H), 7.02 (t, J = 8.7 Hz, 2H), 3.59 (d, $J_{H\text{-}P}$ = 11.5 Hz, 6H), 3.14 (br s, 1H), 1.58 -1.77 (m, 5H), 1.12 – 1.35 (m, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.7 (CO), 162.6 (d, $J_{C\text{-}F}$ = 246.0 Hz, C_{Ar}), 131.7 ($C_{Ar}H$), 131.6 ($C_{Ar}H$), 128.6 (d, $J_{C\text{-}P}$ = 19.5 Hz, C_{pyr}), 126.6 (d, $J_{C\text{-}F}$ = 3.2 Hz, C_{Ar}), 114.9 ($C_{Ar}H$), 114.7 ($C_{Ar}H$), 53.2 (d, $J_{C\text{-}P}$ = 5.5 Hz, {PO}OCH_3 x 2), 46.9 ($CH_{aliphatic}$), 28.7 (CH_2 x 2), 25.8 (CH_2), 25.5 (CH_2 x 2); ^{31}P NMR (161.9 MHz, $CDCl_3$) δ 8.84; MS (ES+) m/e (rel intensity): 381.1 (MH^+, 100), 382.1 (19); HRMS for $C_{18}H_{22}FN_2O_4P$: calcd. (MH^+): 381.1379, found: 381.1372.

*Dimethyl 3-isobutyryl-4-phenyl-1H-pyrazol-5-ylphosphonate (**3l**)*

Colorless solid; isolated yield 85% (274 mg). R_f 0.30 (70% EtOAc/hexane); Mp 148-150 °C; IR (KBr, cm^{-1}): 3126 (m), 2971 (m), 1691 (s), 1237 (s), 1033 (s), 950 (m); ^{1}H NMR (400 MHz $CDCl_3$) δ 12.69 (br s, 1H), 7.27 – 7.33 (m, 5H), 3.56 (d, J_{H-P} = 11.6 Hz, 6H), 3.38 - 3.44 (m, 1H), 1.04 (d, J = 6.8 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.6 (CO), 130.8 (C_{Ar}), 129.8 (C_{Ar}H x 2), 129.6 (C_{pyr}), 128.0 (C_{Ar}H), 127.7 (C_{Ar}H x 2), 53.3 (d, J_{C-P} = 5.4 Hz, {PO}OCH_3 x 2), 37.1 ($CH_{aliphatic}$), 18.5 (CH_3 x 2); ^{31}P NMR (161.9 MHz, $CDCl_3$) δ 8.86; MS (ES+) m/e (rel intensity): 323.1 (MH^+, 100), 324.1 (18); HRMS for $C_{15}H_{19}N_2O_4P$: calcd. (MH^+): 323.1161, found: 323.1161.

*Dimethyl 3-(3-methylbutanoyl)-4-phenyl-1H-pyrazol-5-ylphosphonate (**3m**)*

Colorless solid; isolated yield 88% (296 mg). R_f 0.30 (70% EtOAc/hexane); Mp 118-120 °C; IR (KBr, cm^{-1}): 3126 (m), 2957 (m), 1690 (s), 1238 (s), 1035 (s), 786 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 – 7.34 (m, 5H), 3.56 (d, J_{H-P} = 11.6 Hz, 6H), 2.64 (br s, 2H), 2.05 – 2.14 (m, 1H), 0.79 (d, J = 6.6 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.8 (CO), 130.7 (C_{Ar}), 129.9 (C_{Ar}H x 2), 129.7 (C_{pyr}), 129.3 (d, J_{C-P} = 19.1 Hz, C_{pyr}), 128.3 (C_{Ar}H), 127.9 (C_{Ar}H x 2), 126.4 (C_{pyr}), 53.3 (d, J_{C-P} = 5.7 Hz, {PO}OCH_3 x 2), 48.9 ($CH_{aliphatic}$), 24.7 (CH_2), 22.6 (CH_3 x 2); ^{31}P NMR (161.9 MHz, $CDCl_3$) δ 9.04; MS (ES+) m/e (rel intensity): 337.1 (MH^+, 100), 338.1 (20); HRMS for $C_{16}H_{21}N_2O_4P$: calcd. (MH^+): 337.1317, found: 337.1314.

*Dimethyl 3-hexanoyl-4-phenyl-1H-pyrazol-5-ylphosphonate (**3n**)*

Colorless solid; isolated yield 88% (308 mg). R_f 0.30 (70% EtOAc/hexane); Mp 88-90 °C; IR (KBr, cm^{-1}): 3123 (br m), 2956 (m), 1691 (s), 1239 (s), 1034 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 – 7.33 (m collapsed to appear as doublet, 5H), 3.56 (d, J_{H-P} = 11.5 Hz, 6H), 2.74 (br s, 2H), 1.52 (br s, 2H), 1.18 (br s, 4H), 0.77 (br s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.5 (CO), 130.7 (C_{Ar}), 129.9 (C_{Ar}H x 2), 129.3 (d, J_{C-P} = 17.9 Hz, C_{pyr}), 128.2 (C_{Ar}H), 127.8 (C_{Ar}H x 2), 53.3 (d, J_{C-P} = 4.7 Hz, {PO}OCH_3 x 2), 40.1 (CH_2), 31.3 (CH_2), 23.4 (CH_2), 22.4 (CH_2), 13.8 (CH_3); ^{31}P NMR (161.9 MHz, $CDCl_3$) δ 9.10; MS (ES+) m/e (rel intensity): 351.1 (MH^+, 100), 352.1 (19); HRMS for $C_{17}H_{23}N_2O_4P$: calcd. (MH^+): 351.1474, found: 351.1470.

*Dimethyl 3-benzoyl-1H-pyrazol-5-ylphosphonate (**3o**)*

Brown solid; isolated yield 87% (244 mg). R_f 0.30 (70% EtOAc/hexane); Mp 98-100 °C; IR (KBr, cm^{-1}): 3409 (br m), 3021 (m), 1650 (m), 1216 (s), 1038 (m), 903 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.72 (bs, 1H), 8.05 (d, J = 7.2 Hz, 2H), 7.55 (t, J = 7.4 Hz, 1H), 7.44 (t, J = 7.4 Hz, 2H), 7.28 (d, J = 1.8 Hz, 1H), 3.79 (d, J_{H-P} = 11.4 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 185.8 (CO), 136.6 (C_{Ar}), 133.3 (C_{Ar}H), 129.9 (C_{Ar}H x 2), 128.5 (C_{Ar}H x 2), 115.7 (d, J_{C-P} = 19.6 Hz, C_{pyr}H), 53.6 (d, J_{C-P} = 5.8 Hz, {PO}OCH_3 x 2); ^{31}P NMR (161.9 MHz, $CDCl_3$) δ 9.57; MS (ES+) m/e (rel intensity): 281.0 (MH^+, 100), 282.0 (13); HRMS for $C_{12}H_{13}N_2O_4P$: calcd. (MH^+): 281.0691, found: 281.0679.

*Dimethyl 3-(3-methoxybenzoyl)-1H-pyrazol-5-ylphosphonate (**3p**)*

Colorless solid; isolated yield 86% (267 mg). R_f 0.30 (70% EtOAc/hexane); Mp 80-82 °C; IR (KBr, cm^{-1}): 3415 (br m), 3020 (m), 1648 (m), 1216 (s), 1040 (m), 932 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.69 (br s, 1H), 7.65 (d, J = 7.4 Hz, 1H), 7.54 (s, 1H), 7.33 (t, J = 8.0 Hz, 1H), 7.27 (d, J = 1.9 Hz , 1H), 7.09 (dd, J = 8.2 Hz, 2.5 Hz, 1H), 3.80 (s, 3H), 3.78 (d, J_{H-P} = 9.7 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 185.6 (CO), 159.6 (C_{Ar}), 137.8 (C_{Ar}), 129.4 (C_{Ar}H), 122.6 (C_{Ar}H), 119.6 (C_{Ar}H), 115.7 (d, J_{C-P} = 20.4 Hz, C_{pyr}H), 114.2 (C_{Ar}H), 55.4 (OCH_3), 53.5 (d, J_{C-P} = 5.5 Hz, {PO}OCH_3 x 2); ^{31}P NMR (161.9 MHz, $CDCl_3$) δ 9.64; MS (ES+) m/e (rel intensity): 311.0 (MH^+, 100), 312.0 (15); HRMS for $C_{13}H_{15}N_2O_5P$: calcd. (MH^+): 311.0797, found: 311.0785.

*Dimethyl 3-(furan-2-carbonyl)-1H-pyrazol-5-ylphosphonate (**3q**)*

Brown solid; Mp 84-86 °C; isolated yield 84% (227 mg). R_f 0.30 (70% EtOAc/hexane); IR (Film, cm^{-1}): 3405 (br m), 3021 (m), 1636 (m), 1216 (s), 1036 (m), 931 (s); ^{1}H NMR (400

MHz, $CDCl_3$) δ 7.70 (d, J = 3.4 Hz, 1H), 7.65 (s, 1H), 7.48 (d, J = 1.8 Hz, 1H), 6.54 (dd, J = 3.5 Hz, 1.5 Hz, 1H), 3.78 (d, $J_{H\text{-}P}$ = 11.5 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.1 (CO), 151.3 (C_{fur}), 147.7 ($C_{fur}H$), 121.5 ($C_{fur}H$), 115.3 (d, $J_{C\text{-}P}$ = 19.6 Hz, $C_{pyr}H$), 112.7 ($C_{fur}H$), 53.7 ({PO}OCH_3 x 2); ^{31}P NMR (161.9 MHz, $CDCl_3$) δ 9.70; MS (ES+) m/e (rel intensity): 271.0 (MH^+, 100), 272.0 (12); HRMS for $C_{10}H_{11}N_2O_5P$: calcd. (MH^+): 271.0484, found: 271.0473.

*Dimethyl 3-(3-methoxy-3-phenylacryloyl)-4-phenyl-1H-pyrazol-5-ylphosphonate (**3r**)*

Yellow solid; Mp 124-126 °C; isolated yield 79% (325 mg). R_f 0.30 (70% EtOAc/hexane); IR (Film, cm^{-1}): 3414 (br m), 3020 (m), 1611 (m), 1217 (s), 1039 (m), 927 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 – 7.40 (m, 10H), 5.54 (s, 1H), 3.57 (d, $J_{H\text{-}P}$ = 11.2 Hz, 6H), 3.18 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.9 (CO), 173.3 ($C_{aliphatic}$), 134.7 (C_{Ar}), 131.5 (C_{Ar}), 130.6 ($C_{Ar}H$ x 2), 130.3 ($C_{Ar}H$), 128.8 ($C_{Ar}H$ x 2), 128.4 ($C_{Ar}H$), 128.3 ($C_{Ar}H$ x 2), 127.8 ($C_{Ar}H$ x 2), 127.5 (C_{pyr}), 98.8 ($CH_{aliphatic}$), 56.0 (OCH_3), 53.1 (d, $J_{C\text{-}P}$ = 5.5 Hz, {PO}OCH_3 x 2); ^{31}P NMR (161.9 MHz, $CDCl_3$) δ 10.77; MS (ES+) m/e (rel intensity): 412.9 (MH^+, 100), 413.0 (23); HRMS for $C_{21}H_{21}N_2O_5P$: calcd. (MH^+): 413.1266, found: 413.1257.

*Dimethyl 3-(4-(3-methoxy-3-phenylacryloyl)benzoyl)-4-phenyl-1H-pyrazol-5-ylphosphonate (**3s**)*

Light yellow solid; isolated yield 81% (418 mg). R_f 0.30 (70% EtOAc/hexane); Mp 98-100 °C; IR (KBr, cm^{-1}): 3396 (br m), 3022 (m), 1621 (m), 1216 (s), 1035 (m), 929 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.4 (br s, 1H), 7.75 – 7.89 (m, 4H), 7.26 – 7.36 (m, 10H), 6.09 (s, 1H), 3.86 (s, 3H), 3.59 (d, $J_{H\text{-}P}$ = 11.5 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 189.7 (CO), 187.6 (CO), 172.4 ($C_{aliphatic}$), 142.9 (C_{Ar}), 139.5 (C_{Ar}), 135.5 (C_{Ar}), 135.0 (C_{Ar}), 130.3 ($C_{Ar}H$ x 2), 130.1 ($C_{Ar}H$), 129.9 ($C_{Ar}H$ x 2), 128.9 ($C_{Ar}H$ x 2), 128.6 (C_{pyr}), 128.1 ($C_{Ar}H$ x 2), 127.9 ($C_{Ar}H$ x 4), 127.8 ($C_{Ar}H$ x 2), 98.2 ($CH_{aliphatic}$), 56.6 (OCH_3), 53.4 (d, $J_{C\text{-}P}$ = 5.5 Hz, {PO}OCH_3 x 2); ^{31}P NMR (161.9 MHz, $CDCl_3$) δ 8.53; MS (ES+) m/e (rel intensity): 517.1 (MH^+, 100), 518.1 (30); HRMS for $C_{28}H_{25}N_2O_6P$: calcd. (MH^+): 517.1528, found: 517.1509.

Acknowledgments

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11. Selected X-Ray Crystallographic data for **3a**, $C_{18}H_{17}N_2O_4P$: M = 356.31, orthorhombic, Pbca, a = 31.101(7) Å, b = 16.501(4) Å, c = 13.381(3) Å, V = 1804.7(3)Å^3, α = 90.00°, β = 90.00°, γ = 90.00°, Z = 16, D_c = 1.379 g cm^{-3}, μ (Mo-Kα) = 0.186 mm^{-1}, F(000) = 2976, Reflections Collected: unique 6246/5851 [R(int) = 0.0519]. Final R indices [I>2σ(I)], R1 = 0.0453, wR_2 = 0.1303, R indices (all data), R1 = 0.0528, wR_2 = 0.1449.
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Supplementary Material

The copies of the ^{1}H NMR, ^{13}C NMR and ^{31}P NMR spectra for the products are available.