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Highly Selective Synthesis of Pyrazole and Spiropyrazoline Phosphonates via Base-Assisted Reaction of the Bestmann−Ohira Reagent with Enones§

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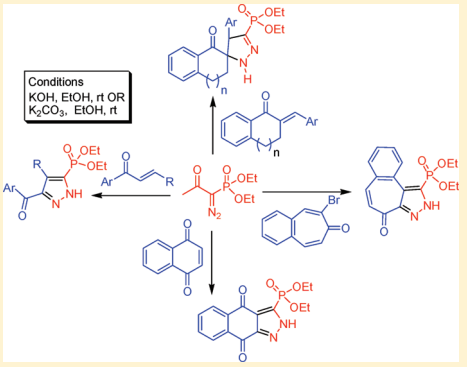
Supporting Information

ABSTRACT: Novel carbonylated pyrazole phosphonates have been synthesized as single regioisomers by treating conjugated enones, dienones, tropone, and quinone with the Bestmann−Ohira reagent under KOH/EtOH conditions at room temperature. Through an "interrupted" version of the above reaction, carbonylated spiropyrazoline phosphonates have been synthesized from arylidenecycloalkanones under similar conditions (K_2CO_3/EtOH) with absolute regio- and diastereoselectivity. The key structures were confirmed by detailed spectroscopic analysis and X-ray crystallography.

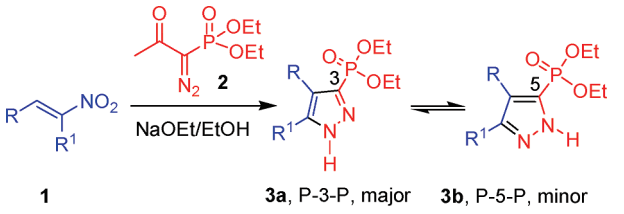


Pyrazoles are distinguished by their properties as biological agents[1] and ligands in synthesis.[2] The biological properties of organophosphorus compounds,[3] in particular, the carboxylate mimicking ability of the phosphonate moiety, are also well-documented in the literature.[4] The methods reported for the synthesis of phosphonylpyrazoles via 1,3-dipolar cycloaddition of diazoalkanes with alkynes[5] and the reaction of 1,3-difunctional compounds with hydrazines[6] involve multistep reaction sequences and sometimes proceed with poor yield and regioselectivity.

Recently, we reported a regioselective synthesis of phosphonylpyrazoles **3** via reaction of Bestmann−Ohira reagent (BOR) **2**[7] with a variety nitroalkenes and nitrodienes **1** mediated by NaOEt in EtOH at room temperature (Scheme 1).[8] Besides pyrazoles **3** possessing multiple functionalities, pyrazoles fused to carbocycles and heterocycles have been synthesized by this method, demonstrating for the first time the reactivity of (BOR) **2** as a cycloaddition partner in organic synthesis. The solvent and the temperature dependence of the tautomerism exhibited by phosphonylpyrazoles **3** has been extensively investigated by NMR using ^{1}H and ^{31}P as the probe nuclei. Application of our methodology to other dipolarophiles, such as acrylonitrile,[9] and dipoles, such as diazoester,[10] has been recently reported.

We envisioned that facile synthesis of novel carbonylated phosphonylpyrazoles would be possible by reacting BOR **2** with α,β-unsaturated carbonyl compounds such as enones. Thus, chalcone **4a** was treated with BOR **2** in the presence of different bases in EtOH at rt to afford pyrazole **5a** (Table 1). First of all, the conditions employed in the reaction of BOR **2** with nitroalkenes

Scheme 1



(NaOEt/EtOH, entry 1, Table 1)[8] and in the well-established one-carbon homologation of aldehydes to acetylenes (K_2CO_3/EtOH, entry 2, Table 1)[11] were screened. While the above conditions (entries 1 and 2) and Cs_2CO_3/EtOH (entry 3) did indeed provide the desired product in good yield, other alkali metal carbonates were ineffective for our reaction (entries 4 and 5, Table 1). Finally, KOH/EtOH was found to be superior both in terms of the reaction time and the isolated yield (entry 6, Table 1).

The above optimized conditions were employed for the reaction of BOR **2** with chalcones **4b−g** (Table 2). It may be noted that, besides parent chalcone **4a** (entry 1), a chalcone possessing a weakly electron-donating substituent **4e** (entry 5) provided corresponding phosphonylpyrazole in >90% yield (Table 2). On the other hand, the yields of phosphonylpyrazoles **5b−d** and **5g** obtained from chalcones possessing stronger

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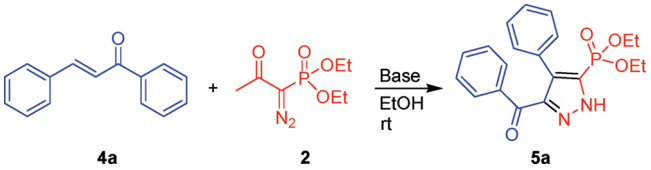
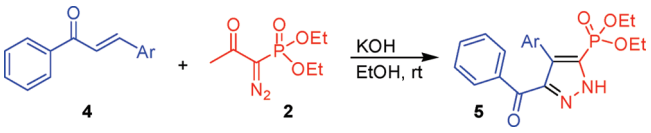
Table 1. Phosphonylpyrazole 5a from Chalcone 4a and Bestmann−Ohira Reagent 2: Base Screening[a]



entry	base/solvent	time (h)	% yield[b]
1	NaOEt/EtOH	6	88[c]
2	K_2CO_3/EtOH	24	85[c]
3	Cs_2CO_3/EtOH	19	83[c]
4	Na_2CO_3/EtOH	48	35[d]
5	Li_2CO_3/EtOH	48	15[e]
6	KOH/EtOH	2	92

[a] **4a** and **2** were used in 1:1.4 ratio, and the reactions were performed at 0.5 mmol scale; 2 equiv of base was used. [b] Isolated yield after silica gel column chromatography. [c] Traces (2−3%) of chalcone were recovered. [d] 55% of **4a** was recovered. [e] 70% of **4a** was recovered.

Table 2. Synthesis of Phosphonylpyrazoles 5 from Chalcones 4 and Bestmann−Ohira Reagent 2[a]



entry	chalcone 4	Ar	time (h)	% yield[b]
1	**4a**	Ph	2	92[c]
2	**4b**	4-OMe-Ph	6	82[d]
3	**4c**	3,4,5-$(OMe)_3$-Ph	5	85
4	**4d**	4-NMe_2-Ph	20	77[d]
5	**4e**	4-Cl-Ph	2	93
6	**4f**	4-NO_2	1	85
7	**4g**	2-thienyl	6	83

[a] **4** and **2** were used in 1:1.4 ratio, and the reactions were performed at 0.5 mmol scale; 2 equiv of base was used. [b] Isolated yield after silica gel column chromatography. [c] 94% yield in 1 min under MW irradiation conditions, 95% yield at 5 mmol scale under conventional conditions. [d] Traces (3−4%) of chalcone **4** were recovered.

electron-donating substituents **4b−d** and **4g**, respectively, are marginally less (entries 2−4 and 7). In particular, a strongly electron-donating group such as NMe_2 substantially reduces the reactivity of chalcone as reflected in the reaction time (20 h) and isolated yield (77%, entry 4, Table 2). Interestingly, chalcone possessing a strongly electron-withdrawing substituent such as NO_2 (e.g., **4f**) gives rise to the desired pyrazole **5f** in marginally lower yield (85%, entry 6, Table 2). Therefore, it appears reasonable to conclude that strongly electron-donating and -withdrawing substituents in conjugation with the reacting π system reduce the reactivity of chalcone and provide the product in slightly lower yield. The structure of **5a−g** was unambiguously established by single-crystal X-ray analysis of a representative compound **5e** (see Experimental Section and the Supporting Information).

Scheme 2

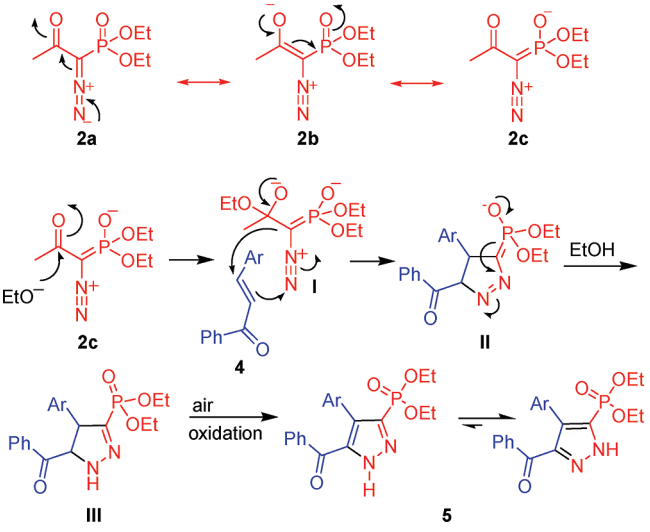
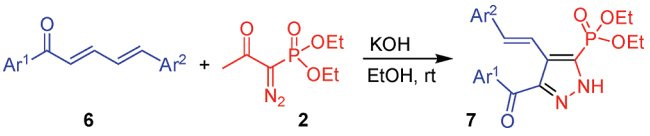


Table 3. Synthesis of Phosphonylpyrazoles 7 from Dienones 6 and Bestmann−Ohira Reagent 2[a]



entry	dienone 6	Ar^1	Ar^2	time (h)	% yield[b]
1	**6a**	Ph	Ph	6	85
2	**6b**	4-Me-Ph	Ph	7	88
3	**6c**	4-Cl-Ph	Ph	4	89
4	**6d**	Ph	2-furyl	5	80

[a] **6** and **2** were used in 1:1.4 ratio, and the reactions were performed at 0.5 mmol scale; 2 equiv of base was used. [b] Isolated yield after silica gel column chromatography.

The proposed mechanism involves prior deacylation of BOR **2** by the nucleophilic alkoxide followed by reaction of the diazophosphonate anion arising from **I**[8] with enone **4** in a 1,3-dipolar fashion to afford the initial cycloadduct **II** (Scheme 2). Subsequent protonation of **II** to form pyrazoline **III** and its aromatization via air oxidation completes the reaction. Our earlier studies on the reaction of BOR **2** with nitroalkenes confirmed that the 1,3-dipolar cycloaddition does not take place before deacylation because, in the absence of base and protic solvent, there was no reaction at all.[8] The 100% diastereoselectivity observed in the pyrazoline formation (vide infra) suggests that the cycloaddition could be concerted, as shown in our mechanism (Scheme 2).

After synthesizing phosphonylpyrazoles **5** containing an aryl group and a benzoyl group on adjacent carbons, we investigated the reactivity of dienones **6** with BOR **2** under the optimized conditions (Table 3). In general, the reactions were complete in 7 h or less, and pyrazole phosphonates with a benzoyl group and a styrenyl group at vicinal carbons were isolated in excellent yield (80−89%, entries 1−4, Table 3).

The above conditions were successfully employed in the synthesis of more complex pyrazoles **9** and **11** in good yield

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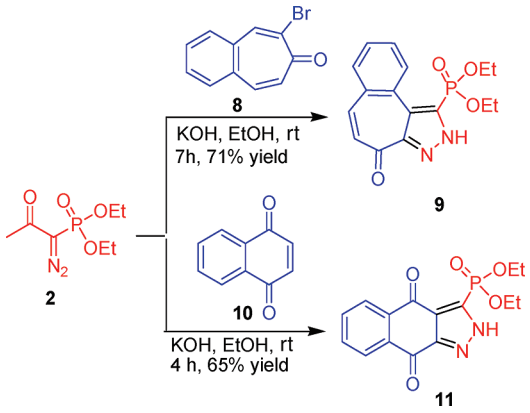
Scheme 3



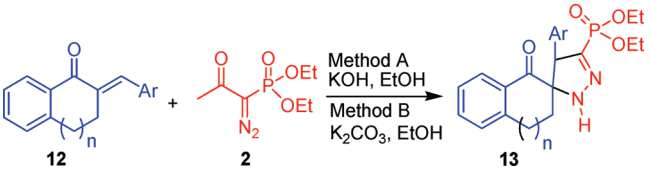
(65−71%) from bromobenzotropone **8** and benzoquinone **10** (Scheme 3). In the case of **8**, the initial cycloadduct pyrazoline presumably undergoes HBr elimination to afford pyrazole **9**. These representative examples show further scope of the reaction.

Having synthesized a variety of pyrazole phosphonates from enones **4**, dienones **6**, tropone **8**, and quinone **10**, we turned our attention to "interrupt" the reaction of BOR **2** with enones at the pyrazoline stage by appropriate choice of enone such as **12**. The potential biological properties of pyrazolines such as antifungal,[12] antidepressant,[13,14] anticonvulsant,[14] anti-inflammatory,[15] antibacterial,[16] and antitumor[17] properties have been well-recognized. There are sporadic reports of synthesis of spiro-1-pyrazolines by the 1,3-dipolar cycloaddition of exocyclic α,β-unsaturated ketones and diazomethane.[18] Recently, Molchanov et al. have reported the synthesis of spiropyrazolines in moderate yield by the addition of diazomethane and ethyl diazoacetate to 2-arylidene-1-tetralones.[19] Spiropyrazolines were also synthesized by the reaction of 2-arylidene indan-1,3-diones with in situ generated *C,N*-diarylnitrilimines.[20] However, the only report, to our knowledge, on the synthesis of a spiropyrazoline phosphonate relies on the reaction between an active methylene phosphonate and a diazodiketone.[21]

In view of the above, we treated chalcones **12** with BOR **2** under the established conditions (KOH/EtOH) to generate pyrazolines **13** (method A, Table 4). However, the yields were moderate and the reaction remained incomplete in the case of **12a**−**d** (n =1, entries 1−4, method A) even after allowing considerable reaction time (Table 4). In the case of five-membered analogues (n = 0, entries 5 and 6, method A), although the reactions were complete in 20−30 min, the yield remained moderate (Table 4). Initially, it appeared that the poor reactivity of **12** was due to the α-substitution and the conformationally locked structure. However, we decided to expose chalcones **12** and BOR **2** to alternative reaction conditions to see whether the yields could be improved. Thus treatment of chalcones **12** with BOR **2** in the presence of K_2CO_3 in EtOH improved the yields substantially, which ruled out the possibility of structural features of chalcones **12** being responsible for the incomplete reaction and lower yield with method A.[22]

Quite remarkably, pyrazolines **13a**−**f** were formed as single diastereomers in our reaction. Examination of the X-ray data of **13c** showed that the carbonyl oxygen and pyrazoline nitrogen (CO−C−C−NH) are at a dihedral angle close to 90° (88.2°), while the dihedral angle between carbonyl oxygen and the benzylic

Table 4. Synthesis of Spiropyrazolines 13 from Chalcones 12 and Bestmann−Ohira Reagent 2[a]

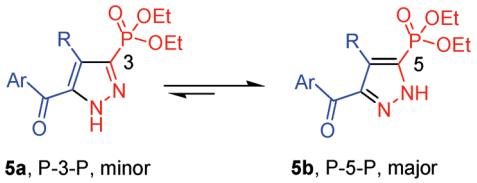


				method A		method B	
entry	**12**	n	Ar	time	% yield[b]	time	% yield[b,d]
1	**12a**	1	Ph	22 h	61[c]	28 h	72
2	**12b**	1	4-OMe-Ph	24 h	56[c]	24 h	76
3	**12c**	1	4-Cl-Ph	7 h	75[c]	22 h	91
4	**12d**	1	2-thienyl	24 h	51[c]	26 h	70
5	**12e**	0	Ph	30 min	50	6 h	72
6	**12f**	0	4-Cl-Ph	20 min	52	6 h	74

[a] **12** and **2** were used in 1:1.4 ratio, and the reactions were performed at 0.5 mmol scale; 2 equiv of base was used. [b] Isolated yield after silica gel column chromatography. [c] 2−20% of **12** was recovered. [d] 4−21% of **12** was recovered.

carbon of pyrazoline is closer to 0° (−20.3°). This suggested that the possible repulsion between the lone pairs of carbonyl oxygen and pyrazoline nitrogen is avoided during the cycloaddition and in the product. It is also important to note that a quaternary spiro center is generated in this highly diastereoselective cycloaddition.

Pyrazoles **3** derived from nitroalkenes **1**, particularly those in which R^1 = H, exhibited tautomerism between pyrazole 3-phosphonate (P-3-P) **3a** and pyrazole 5-phosphonate (P-5-P) **3b** (Scheme 1).[8] Extensive solvent and temperature-dependent ^{1}H and ^{31}P NMR studies have shown that **3a** is more stable than **3b**, and the single-crystal X-ray analysis showed the existence of only **3a** in solid state.[8] In contrast to the above observations, none of the pyrazole phosphonates **5**, **7**, **9**, and **11** derived, respectively, from enones **4**, **6**, **8**, and **10** exhibited tautomerism on ^{1}H or ^{31}P NMR time scale. Furthermore and in stark contrast to the behavior of pyrazole **3** derived from nitroalkenes **1**, pyrazoles **5** derived from enones **4** were stabilized as pyrazole 5-phosphonates **5b** as evident from X-ray analysis (see Experimental Section and the Supporting Information).



In tautomer **5a**, the diazophosphonate and the enone moieties are independently stabilized by resonance and both the benzoyl group and the phosphonate are cross-conjugated with the pyrazole π system, leading to an overall destabilization of the fused structure. On the other hand, in tautomer **5b**, the diazoenone and the α,β-unsaturated phosphonate moieties, the latter further conjugated in most cases, are resonance stabilized and the pyrazole π system is in full conjugation with phosphonate, rendering the annulated structure **5b** relatively more stabilized

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in comparison with **5a**. This qualitative comparison of relative stabilities of tautomers **5a** and **5b** explains the structure as confirmed by single-crystal X-ray analysis. By analogy, pyrazoles **7**, **9**, and **11** are also likely to remain as pyrazole 5-phosphonates.

In conclusion, 1,3-dipolar cycloaddition of the Bestmann–Ohira reagent with α,β-unsaturated ketones in the presence of KOH/EtOH afforded pyrazole phosphonates as single regioisomers in good to excellent yield. Similar reaction involving α-arylidenecycloalkanones led to the formation of spiropyrazoline phosphonates as single regio- and diastereomers in high yield under K_2CO_3/EtOH conditions. The structures were unambiguously established by single-crystal X-ray analysis which suggested the existence of pyrazole phosphonates as pyrazole 5-phosphonate tautomers in solid state.

EXPERIMENTAL SECTION

General. The melting points recorded are uncorrected. NMR spectra (^{1}H, ^{1}H decoupled ^{13}C, ^{1}H–^{1}H COSY, and ^{31}P) were recorded with TMS as the internal standard for ^{1}H and ^{13}C and phosphoric acid as the external standard for ^{31}P. The coupling constants (J values) are given in hertz. High-resolution mass spectra were recorded at 60–70 eV under ESI Q-TOF conditions. X-ray data were collected on a Nonius MACH 3 diffractometer equipped with graphite monochromated Mo Kα radiation. The structure was solved by direct methods with SHELXS97 and refined by full-matrix least-squares against F^2 using SHELXL97 software. Chalcones **4**,[23] dienones **6**,[24] tropone **8**,[25] and enones **12**[26] were prepared following literature protocols.

General Procedure for the Synthesis of Pyrazoles 5, 7, 9, 11, and Pyrazoline 13. To a stirred solution of chalcones **4**, dienones **6**, tropone **8**, quinone **10**, or enones **12** (0.5 mmol) and BOR **2** (0.7 mmol, 0.154 g) in dry EtOH (10 mL) was added KOH (1.0 mmol, 0.056 g) at rt, and the resulting mixture was stirred until the reaction was complete (see Tables 2–4). The crude residue was directly purified by silica gel column chromatography without any workup to afford pure pyrazole **5**, **7**, **9**, **11**, or pyrazoline **13**.

Note: In the case of chalcone **4a**, the above reaction was carried out at 5 mmol scale under conventional conditions and also at 0.5 mmol scale under microwave irradiation (40 °C, 500 W) conditions (see Table 2, footnote).

Alternative Procedure for the Synthesis of Pyrazolines 13. To a stirred solution of enone **12** (0.5 mmol) and BOR **2** (0.7 mmol, 0.154 g) in dry EtOH (10 mL) was added K_2CO_3 (1.0 mmol, 0.138 g) at room temperature, and the resulting mixture was stirred at rt until the reaction was complete (see Table 4, method B). The crude residue was directly purified by silica gel column chromatography without any workup to afford pure pyrazoline **13**.

Note: Enones, sparingly soluble at room temperature, were dissolved in EtOH by heating at 50–60 °C for 10–15 min.

Diethyl 3-Benzoyl-4-phenyl-1*H*-pyrazol-5-ylphosphonate (5a): Light yellow solid; yield 0.5 mmol scale, conventional conditions, 177 mg, 92%; microwave conditions, 181 mg, 94%; 5 mmol scale, conventional conditions, 1.824 g, 95%; mp 132–133 °C; IR (KBr, cm^{-1}) 3539 (br, w), 3244 (br, m), 2986 (m), 2911 (m), 1658 (m), 1450 (s), 1226 (s), 1026 (s), 908 (m), 697 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.15 (t, J = 7.0 Hz, 6H), 3.95–4.17 (m, 4H), 7.24–7.40 (m, 7H), 7.46–7.53 (m, 1H), 7.99 (d, J = 7.2 Hz, 2H), 13.68 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.0 (d, J_{C-P} = 6.9 Hz), 63.4 (d, J_{C-P} = 5.3 Hz), 127.87, 127.91, 128.1, 129.4, 130.2, 130.4, 130.6, 130.9, 133.0, 137.3, 188.7; ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$) δ 4.21; MS (ES+) m/e (rel intensity) 385 (MH^+, 100), 249 (65), 171 (8); HRMS (ES+) calcd for $C_{20}H_{22}N_2O_4P$ (MH^+) 385.1317, found 385.1330.

Diethyl 3-Benzoyl-4-(4-methoxyphenyl)-1*H*-pyrazol-5-ylphosphonate (5b): Light yellow solid; yield 170 mg, 82%; mp 134–135 °C; IR (KBr, cm^{-1}) 3464 (br, s), 3104 (s), 2957 (s), 2912 (s), 1659 (s), 1612 (s), 1597 (s), 1514 (m), 1470 (m), 1449 (m), 1434 (m), 1406 (m), 1224 (vs), 1191 (vs), 1179 (vs), 1032 (vs), 907 (s), 832 (m), 757 (m); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.18 (t, J = 7.0 Hz, 6H), 3.81 (s, 3H), 3.96–4.17 (m, 4H), 6.86 (d, J = 8.8 Hz, 2H), 7.33 (d, J = 8.8 Hz, 2H), 7.35–7.40 (m, 2H), 7.49–7.53 (m, 1H), 7.98 (d, J = 7.6 Hz, 2H), 13.07 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.1 (d, J_{C-P} = 6.9 Hz), 55.4, 63.4 (d, J_{C-P} = 5.3 Hz), 113.4, 123.0, 128.2, 130.2 (d, J_{C-P} = 18.4 Hz), 130.6, 131.5, 133.1, 137.4, 159.5, 188.9; ^{31}P{^{1}H} NMR (121.4 MHz, $CDCl_3$) δ 4.36; MS (ES+) m/e (rel intensity) 415 (MH^+, 10); HRMS (ES+) calcd for $C_{21}H_{24}N_2O_5P$ (MH^+) 415.1423, found 415.1414.

Diethyl 3-Benzoyl-4-(3,4,5-trimethoxyphenyl)-1*H*-pyrazol-5-ylphosphonate (5c): White solid; yield 202 mg, 85%; mp 150–151 °C; IR (KBr, cm^{-1}) 3539 (br, m), 3124 (br, m), 2937 (m), 1659 (s), 1586 (s), 1453 (m), 1241 (s), 1127 (s), 1050 (m), 1023 (s), 917 (m); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.19 (t, J = 7.0 Hz, 6H), 3.78 (s, 6H), 3.83 (s, 3H), 4.01–4.20 (m, 4H), 6.67 (s, 2H), 7.34–7.38 (m, 2H), 7.48–7.52 (m, 1H), 7.91 (d, J = 6.8 Hz, 2H), 13.16 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.1 (d, J_{C-P} = 6.9 Hz), 56.2, 61.0, 63.4 (d, J_{C-P} = 5.3 Hz), 107.8, 126.0, 128.2 (× 2), 130.1 (d, J_{C-P} = 19.1 Hz), 130.4, 133.3, 137.2, 137.8, 152.7 (×2), 188.8; ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$) δ 6.60; MS (ES+) m/e (rel intensity) 475 (MH^+, 100); HRMS (ES+) calcd for $C_{23}H_{28}N_2O_7P$ (MH^+) 475.1634, found 475.1658.

Diethyl 3-Benzoyl-4-(4-(dimethylamino)phenyl)-1*H*-pyrazol-5-ylphosphonate (5d): Yellow solid; yield 165 mg, 77%; mp 171–172 °C; IR (KBr, cm^{-1}) 3475 (br, s), 3116 (m), 2981 (m), 2906 (m), 1659 (s), 1615 (s), 1547 (m), 1450 (m), 1352 (m), 1230 (s), 1194 (s), 1174 (s), 1026 (s), 979 (m), 907 (s), 698 (m); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.18 (t, J = 7.0 Hz, 6H), 2.94 (s, 6H), 3.97–4.18 (m, 4H), 6.66 (d, J = 8.4 Hz, 2H), 7.28 (d, J = 8.4 Hz, 2H), 7.34–7.38 (m, 2H), 7.47–7.51 (m, 1H), 7.98 (d, J = 7.6 Hz, 2H), 13.34 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.1 (d, J_{C-P} = 6.9 Hz), 40.6, 63.3 (d, J_{C-P} = 5.4 Hz), 111.9, 118.2, 128.1, 130.6, 131.0 (d, J_{C-P} = 18.3 Hz), 131.0, 132.9, 137.5, 150.3, 189.1; ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$) δ 5.10; MS (ES+) m/e (rel intensity) 428 (MH^+, 100), 400 (4); HRMS (ES+) calcd for $C_{22}H_{27}N_3O_4P$ 428.1739, found 428.1758.

Diethyl 3-Benzoyl-4-(4-chlorophenyl)-1*H*-pyrazol-5-ylphosphonate (5e): Light yellow solid; yield 195 mg, 93%; mp 163–164 °C; IR (KBr, cm^{-1}) 3123 (br, m), 2983 (m), 2909 (m), 1660 (m), 1449 (w), 1423 (w), 1233 (vs), 1198 (m), 1052 (m), 1022 (vs), 909 (m); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.11 (t, J = 7.0 Hz, 6H), 3.90–4.11 (m, 4H), 7.19–7.34 (m, 6H), 7.43–7.48 (m, 1H), 7.93 (d, J = 6.0 Hz, 2H), 13.54 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.1 (d, J_{C-P} = 6.8 Hz), 63.5 (d, J_{C-P} = 5.3 Hz), 128.2, 128.3, 129.3 (d, J_{C-P} = 17.6 Hz), 129.5, 130.6, 131.6, 133.2, 134.1, 137.2, 188.6; ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$) δ 3.92; MS (ES+) m/e (rel intensity) 421 ($[M + 2]H^+$, 25), 419 (MH^+, 100), 391 (3); HRMS (ES+) calcd for $C_{20}H_{21}N_2O_4PCl$ (MH^+) 419.0927, found 419.0915. Selected X-ray data: $C_{20}H_{20}ClN_2O_4P$, M = 418.80, triclinic, space group $P\bar{1}$, a = 9.8119(11) Å, b = 10.4520(12) Å, c = 11.1999(10) Å, β = 73.870(9)°, V = 996.84(18) Å^3, D_c = 1.395 mg/m^3, Z = 2, F(000) = 436, λ = 0.71073 Å, μ = 0.301 mm^{-1}, total/unique reflections = 7382/3504 [R(int) = 0.0436], T = 150 (2) K, θ range = 3.37 to 25.00°, final R [$I > 2\sigma(I)$], $R1$ = 0.0437, $wR2$ = 0.1026; R (all data), $R1$ = 0.0716, $wR2$ = 0.1094 (see also Table S1, Supporting Information).

Diethyl 3-Benzoyl-4-(4-nitrophenyl)-1*H*-pyrazol-5-ylphosphonate (5f): Light yellow solid; yield 183 mg, 85%; mp 130–131 °C; IR (KBr, cm^{-1}) 3116 (s), 2987 (m), 2911 (s), 1659 (s), 1602 (s), 1520 (s), 1450 (m), 1429 (m), 1393 (m), 1348 (s), 1235 (s), 1028 (s), 909 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.19 (t, J = 7.1 Hz, 6H), 4.01–4.21 (m, 4H), 7.38–7.43 (m, 2H), 7.52–7.57 (m, 1H), 7.59 (d, J = 8.9 Hz, 2H), 8.03–8.05 (m, 2H), 8.21 (d, J = 8.9 Hz, 2H), 13.9 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.2 (d, J_{C-P} = 6.0 Hz), 63.8 (d, J_{C-P} = 6.0 Hz), 123.1, 128.4, 130.7, 131.2, 133.5, 137.0, 138.4, 147.4, 152.1, 188.2; ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$) δ 4.98; MS (ES+) m/e (rel intensity) 430

(MH^+, 100), 402 (2), 261 (2), 168 (3); HRMS (ES+) calcd for $C_{20}H_{21}N_3O_6P$ (MH^+) 430.1168, found 430.1153.

Diethyl 3-Benzoyl-4-(thiophen-2-yl)-1*H*-pyrazol-5-ylphosphonate (5g): Light brown solid; yield 162 mg, 83%; mp 136−137 °C; IR (KBr, cm^{-1}) 3436 (br, m), 3095 (m), 2966 (m), 2913 (m), 1657 (s), 1631 (s), 1447 (s), 1423 (s), 1352 (m), 1221 (s), 1021 (s), 899 (s); ^1H NMR (400 MHz, $CDCl_3$) δ 1.22 (t, J = 7.2 Hz, 6H), 4.02−4.22 (m, 4H), 7.01 (dd, J = 5.2, 3.6 Hz, 1H), 7.21 (dd, J = 3.6, 1.2 Hz, 1H), 7.33 (dd, J = 5.2, 1.2 Hz, 1H), 7.37−7.41 (m, 2H), 7.50−7.54 (m, 1H), 8.01 (d, J = 6.8 Hz, 2H), 13.82 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.1 (d, J_{C-P} = 6.8 Hz), 63.6 (d, J_{C-P} = 5.3 Hz), 122.6 (d, J_{C-P} = 18.6 Hz), 126.9, 127.1, 128.2, 129.4, 130.6, 133.2, 137.2, 188.7; $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$) δ 3.53; MS (ES+) m/e (rel intensity) 391 (MH^+, 100); HRMS (ES+) calcd for $C_{18}H_{20}N_2O_4PS$ (MH^+) 391.0881, found 391.0887.

(*E*)-Diethyl 3-Benzoyl-4-styryl-1*H*-pyrazol-5-ylphosphonate (7a): Light yellow solid; yield 175 mg, 85%; mp 135−136 °C; IR (KBr, cm^{-1}) 3489 (br, m), 3128 (m), 2984 (m), 2908 (m), 1654 (vs), 1427 (m), 1231 (vs), 1162 (s), 1019 (vs), 915 (vs); ^1H NMR (400 MHz, $CDCl_3$) δ 1.35 (t, J = 7.0 Hz, 6H), 4.13−4.24 (m, 2H), 4.25−4.34 (m, 2H), 7.24−7.29 (m, 2H), 7.32−7.36 (m, 3H), 7.44−7.52 (m, 4H), 7.55−7.60 (m, 1H), 8.06−8.12 (m, 2H), 13.2 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.3 (d, J_{C-P} = 6.0 Hz), 63.7 (d, J_{C-P} = 5.0 Hz), 117.0, 126.7, 127.7 (d, J_{C-P} = 17.4 Hz), 128.1, 128.3, 128.8, 130.7, 133.0, 134.9, 137.5, 137.9, 147.9, 189.8; $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$) δ 6.77; MS (ES+) m/e (rel intensity) 411 (MH^+, 100), 254 (3); HRMS (ES^+) calcd for $C_{22}H_{24}N_2O_4P$ (MH^+) 411.1474, found 411.1474.

(*E*)-Diethyl 3-(4-Methylbenzoyl)-4-styryl-1*H*-pyrazol-5-ylphosphonate (7b): Light yellow solid; yield 187 mg, 88%; mp 139−140 °C; IR (KBr, cm^{-1}) 3131 (br m), 2984 (m), 2908 (m), 1652 (s), 1606 (m), 1431 (m), 1231 (s), 1162 (m), 1021 (vs), 917 (s); ^1H NMR (400 MHz, $CDCl_3$) δ 1.36 (t, J = 7.0 Hz, 6H), 2.42 (s, 3H), 4.13−4.33 (m, 4H), 7.24−7.28 (m, 3H), 7.31−7.37 (m, 3H), 7.46−7.54 (m, 3H), 8.00 (d, J = 8.4 Hz, 2H), 12.45 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.3 (d, J_{C-P} = 7.0 Hz), 21.8, 63.6 (d, J_{C-P} = 5.0 Hz), 117.1, 126.7, 127.5 (d, J_{C-P} = 17.4 Hz), 128.0, 128.7, 129.0, 130.9, 134.7, 135.3, 137.5, 143.9, 189.4; $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$) δ 6.59; MS (ES+) m/e (rel intensity) 425 (MH^+, 100), 261 (12), 232 (17), 172 (10); HRMS (ES^+) calcd for $C_{23}H_{26}N_2O_4P$ (MH^+) 425.1630, found 425.1645.

(*E*)-Diethyl 3-(4-Chlorobenzoyl)-4-styryl-1*H*-pyrazol-5-ylphosphonate (7c): White solid; yield 198 mg, 89%; mp 107−108 °C; IR (KBr, cm^{-1}) 3121 (br, m), 2984 (w), 2906 (w), 1658 (s), 1588 (m), 1429 (s), 1232 (s), 1162 (s), 1092 (m), 1045 (s), 1018 (vs), 916 (s); ^1H NMR (400 MHz, $CDCl_3$) δ 1.36 (t, J = 7.0 Hz, 6H), 4.13−4.34 (m, 4H), 7.29 (d, J = 8.4 Hz, 1H), 7.31−7.38 (m, 3H), 7.44 (d, J = 8.4 Hz, 2H), 7.48−7.60 (m, 3H), 8.09 (d, J = 8.0 Hz, 2H), 13.11 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.3 (d, J_{C-P} = 7.0 Hz), 63.7 (d, J_{C-P} = 5.0 Hz), 116.9, 126.8, 128.0 (d, J_{C-P} = 17.0 Hz), 128.2, 128.5, 128.8, 132.2, 135.1, 136.3, 137.4, 139.4, 188.4; $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$) δ 6.43; MS (ES+) m/e (rel intensity) 447 ($[M + 2]H^+$, 25), 445 (MH^+, 100), 413 (12), 328 (10), 172 (20); HRMS (ES^+) calcd for $C_{22}H_{23}N_2O_4PCl$ (MH^+) 445.1084, found 445.1079.

(*E*)-Diethyl 3-Benzoyl-4-(2-(furan-2-yl)vinyl)-1*H*-pyrazol-5-ylphosphonate (7d): Yellow solid; yield 160 mg, 80%; mp 154−155 °C; IR (KBr, cm^{-1}) 3132 (m), 3013 (m), 2908 (w), 1652 (m), 1219 (s), 1163 (m), 1022 (vs), 915 (m); ^1H NMR (400 MHz, $CDCl_3$) δ 1.35 (t, J = 7.0 Hz, 6H), 4.12−4.33 (m, 4H), 6.36 (d, J = 3.2 Hz, 1H), 6.40 (dd, J = 3.2, 2.0 Hz, 1H), 7.22 (d, J = 16.4 Hz, 1H), 7.38−7.47 (m, 4H), 7.54−7.59 (m, 1H), 8.06−8.11 (m, 2H), 13.29 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.2 (d, J_{C-P} = 6.9 Hz), 63.6 (d, J_{C-P} = 4.9 Hz), 109.4, 111.6, 114.9, 122.3, 127.3 (d, J_{C-P} = 17.2 Hz), 128.1, 130.6, 132.9, 137.8, 142.6, 153.1, 189.7; $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$) δ 6.38; MS (ES+) m/e (rel intensity) 423 (MNa^+, 98), 401 (MH^+, 100), 249 (15); HRMS (ES^+) calcd for $C_{20}H_{22}N_2O_5P$ (MH^+) 401.1266, found 401.1255.

(4*Z*,6*Z*)-Diethyl 4,5-Benzo-2,8-dihydro-8-oxocyclohepta-[*c*]pyrazol-3-yl-3-phosphonate (9): Light yellow solid; yield 118 mg, 71%; mp 111−112 °C; IR (KBr, cm^{-1}) 3467 (br, m), 2994 (w), 2929 (m), 2857 (w), 1632 (vs), 1391 (m), 1226 (m), 1103 (m), 1015 (s); ^1H NMR (400 MHz, $CDCl_3$) δ 1.32 (td, J = 7.0, 3.3 Hz, 6H), 4.23−4.35 (m, 4H), 6.84 (dd, J = 12.4, 5.2 Hz, 1H), 7.47−7.53 (m, 1H), 7.65−7.72 (m, 3H), 9.04 (dd, J = 8.0, 3.2 Hz, 1H), 13.36 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.3 (d, J_{C-P} = 6.1 Hz), 63.7 (d, J_{C-P} = 6.1 Hz), 125.8 (d, J_{C-P} = 23.7 Hz), 128.5, 129.5, 130.5, 130.7, 131.1, 131.8, 135.7, 141.4 (d, J_{C-P} = 229.4 Hz), 141.9 (d, J_{C-P} = 7.7 Hz), 145.8, 178.6; $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$) δ 9.37; MS (ES+) m/e (rel intensity) 333 (MH^+, 100), 305 (7); HRMS (ES+) calcd for $C_{16}H_{18}N_2O_4P$ (MH^+) 333.1004, found 333.1016.

Diethyl 4,9-Dihydro-4,9-dioxo-2*H*-benzo[*f*]indazol-3-yl-3-phosphonate (11): Light brown solid; yield 109 mg, 65%; mp 155−156 °C; IR (KBr, cm^{-1}) 3456 (br, m), 3060 (w), 2984 (w), 2907 (w), 2846 (w), 1683 (vs), 1588 (m), 1388 (m), 1233 (vs), 1168 (w), 1018 (m), 921 (m), 770 (m); ^1H NMR (400 MHz, $CDCl_3$) δ 1.38 (t, J = 7.0 Hz, 6H), 4.27−4.43 (m, 4H), 7.75−7.81 (m, 2H), 8.24−8.32 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.2 (d, J_{C-P} = 6.1 Hz), 64.5 (d, J_{C-P} = 6.1 Hz), 124.4 (d, J_{C-P} = 17.4 Hz), 127.2, 127.4, 133.5, 133.8, 134.3, 134.5, 136.8, 147.1, 177.7, 178.5; $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$) δ 1.67; MS (ES+) m/e (rel intensity) 357 (MNa^+, 100); HRMS (ES+) calcd for $C_{15}H_{15}N_2O_5PNa$ (MNa^+) 357.0616, found 357.0626.

Diethyl 1-Oxo-4′-phenyl-2′,3,4,4′-tetrahydro-1*H*-spiro[naphthalene-2,3′-pyrazole]-5′-ylphosphonate (13a): Yellow solid; yield method A 125 mg, 61%, method B 148 mg, 72%; mp 102−103 °C; IR (KBr, cm^{-1}) 3243 (br, m), 2983 (m), 2929 (m), 1687 (s), 1600 (m), 1456 (m), 1234 (s), 1025 (vs), 763 (s); ^1H NMR (400 MHz, $CDCl_3$) δ 1.12 (td, J = 7.2, 3.6 Hz, 6H), 2.06−2.15 (m, 2H), 2.70−2.84 (m, 2H), 3.75−3.94 (m, 3H), 3.97−4.07 (m, 1H), 4.45 (s, 1H), 6.75 (br s, 1H), 7.18 (d, J = 8.0 Hz, 1H), 7.20−7.25 (m, 2H), 7.29−7.38 (m, 4H), 7.51−7.53 (m, 1H), 8.04 (dd, J = 8.0, 0.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.0 (2 × d, J_{C-P} = 6.1 Hz), 26.1, 28.0, 57.5 (d, J_{C-P} = 21.3 Hz), 62.4 (d, J_{C-P} = 5.3 Hz), 62.8 (d, J_{C-P} = 5.3 Hz), 73.8 (d, J_{C-P} = 4.5 Hz), 127.2, 128.2, 128.7, 128.8, 128.9, 129.5, 129.9, 134.2, 134.8, 142.8, 148.1 (d, J_{C-P} = 225.0 Hz), 195.5; $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$) δ 7.52; MS (ES+) m/e (rel intensity) 414 ($[M + 2]^+$, 25), 413 (MH^+, 100); HRMS (ES+) calcd for $C_{22}H_{26}N_2O_4P$ (MH^+) 413.1630, found 413.1633.

Diethyl 4′-(4-Methoxyphenyl)-1-oxo-2′,3,4,4′-tetrahydro-1*H*-spiro[naphthalene-2,3′-pyrazole]-5′-ylphosphonate (13b): Yellow solid; yield method A 124 mg, 56%, method B 168 mg, 76%; mp 116−117 °C; IR (KBr, cm^{-1}) 3436 (br, s), 2984 (w), 2930 (m), 1686 (s), 1601 (w), 1512 (m), 1247 (vs), 1028 (vs), 758 (vs); ^1H NMR (400 MHz, $CDCl_3$) δ 1.14 (td, J = 7.0, 0.6 Hz, 3H), 1.17 (td, J = 7.2, 0.6 Hz, 3H), 2.05−2.17 (m, 2H), 2.71−2.88 (m, 2H), 3.78−3.98 (m, 3H), 3.81 (s, 3H), 4.00−4.08 (m, 1H), 4.41 (s, 1H), 6.70 (br s, 1H), 6.87 (d, J = 8.7 Hz, 2H), 7.14 (d, J = 8.7 Hz, 2H), 7.17 (dd, J = 7.9, 1.0 Hz, 1H), 7.36 (ddd collapsed to poorly resolved td, J = 7.9, 1.0 Hz, 1H), 7.51 (ddd collapsed to td, J = 7.9, 1.2 Hz, 1H), 8.03 (dd, J = 7.9, 1.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.0 (2 × d, J_{C-P} = 6.8 Hz), 26.0, 28.0, 55.2, 56.8 (d, J_{C-P} = 21.2 Hz), 62.4 (d, J_{C-P} = 5.2 Hz), 62.6 (d, J_{C-P} = 5.3 Hz), 73.6 (d, J_{C-P} = 4.5 Hz), 114.0, 126.7, 126.9, 128.7, 128.8, 129.8, 130.5, 134.1, 142.9, 147.7 (d, J_{C-P} = 225.3 Hz), 159.4, 195.6; $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$) δ 7.62; MS (ES+) m/e (rel intensity) 443 (MH^+, 100); HRMS (ES+) calcd for $C_{23}H_{28}N_2O_5P$ (MH^+) 443.1736, found 443.1727.

Diethyl 4′-(4-Chlorophenyl)-1-oxo-2′,3,4,4′-tetrahydro-1*H*-spiro[naphthalene-2,3′-pyrazole]-5′-ylphosphonate (13c): Yellow solid; yield method A 167 mg, 75%, method B 203 mg, 91%; mp 134−135 °C; IR (KBr, cm^{-1}) 3469 (br, w), 3220 (m), 2985 (m), 2929 (m), 1685 (s), 1600 (m), 1491 (m), 1233 (s), 1023 (s); ^1H NMR (400 MHz, $CDCl_3$) δ 1.15 (td, J = 7.0, 4.0 Hz, 6H), 2.07 (t, J = 6.2 Hz, 2H), 2.79 (t, J = 6.2 Hz, 2H), 3.84−3.96 (m, 3H), 3.98−4.10 (m, 1H), 4.46 (s, 1H), 6.76 (br s, 1H), 7.16 (d, J = 8.3 Hz, 2H), 7.18 (dd, J = 7.3, 1.0 Hz, 1H), 7.32 (d, J = 8.3 Hz, 2H), 7.36 (ddd collapsed to td, J = 7.3, 1.0 Hz, 1H), 7.52

(ddd collapsed to td, J = 7.3, 1.4 Hz, 1H), 8.02 (dd, J = 7.3, 1.4 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.9, 25.9, 27.8, 56.5 (d, J_{C-P} = 21.2 Hz), 62.3 (d, J_{C-P} = 5.3 Hz), 62.6 (d, J_{C-P} = 5.3 Hz), 73.4 (d, J_{C-P} = 4.6 Hz), 127.0, 128.6, 128.7 (× 2), 129.5, 130.6, 133.3, 133.8, 134.1, 142.5, 147.4 (d, J_{C-P} = 219.2 Hz), 194.7; ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$) δ 7.38; MS (ES+) m/e (rel intensity) 449 ([M + 2]H$^+$, 25), 447 (MH$^+$, 100); HRMS (ES+) calcd for $C_{22}H_{25}N_2O_4PCl$ (MH$^+$) 447.1240, found 447.1224. Selected X-ray data for **13c**: $C_{22}H_{24}ClN_2O_4P$, M = 446.85, monoclinic, space group $P21/c$, a = 7.7469(3) Å, b = 23.8598(7) Å, c = 11.6208(4) Å, β = 92.848(3)°, V = 2145.33(13) Å^3, D_c = 1.383 mg/m^3, Z = 4, $F(000)$ = 936, λ = 0.71073 Å, μ = 0.284 mm^{-1}, total/unique reflections = 15487/3768 [R(int) = 0.0647], T = 150 (2) K, θ range = 3.35 to 25.00°, final R [$I > 2\sigma(I)$], $R1$ = 0.0383, $wR2$ = 0.0951; R (all data), $R1$ = 0.0524, $wR2$ = 0.0988 (see also Table S2 Supporting Information).

Diethyl 1-Oxo-4′-(thiophen-2-yl)-2′,3,4,4′-tetrahydro-1*H*-spiro[naphthalene-2,3′-pyrazole]-5′-ylphosphonate (13d): Yellow solid; yield method A 107 mg, 51%, method B 147 mg, 70%; mp 122−123 °C; IR (KBr, cm^{-1}) 3234 (br, m), 2982 (m), 2929 (m), 1683 (s), 1600 (w), 1455 (m), 1233 (vs), 1024 (vs); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.19 (t, J = 7.0 Hz, 6H), 2.10−2.20 (m, 1H), 2.25−2.33 (m, 1H), 2.82−2.92 (m, 1H), 2.96−3.10 (m, 1H), 3.83−4.10 (m, 4H), 4.88 (s, 1H), 6.77 (br s, 1H), 6.95−7.02 (m, 2H), 7.20 (d, J = 7.6 Hz, 1H), 7.24−7.29 (m, 1H), 7.35 (t, J = 7.6 Hz, 1H), 7.52 (ddd collapsed to td, J = 7.6, 1.3 Hz, 1H), 8.01 (dd, J = 7.6, 1.3 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.1 (d, J_{C-P} = 6.1 Hz), 26.4, 28.0, 51.9 (d, J_{C-P} = 21.2 Hz), 62.6 (d, J_{C-P} = 6.1 Hz), 62.9 (d, J_{C-P} = 5.3 Hz), 73.6 (d, J_{C-P} = 4.5 Hz), 125.9, 127.2 (d, J_{C-P} = 6.1 Hz), 128.3, 128.9 (×2), 129.9, 134.3, 136.2, 142.8, 145.9, 148.9, 194.8; ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$) δ 7.08; MS (ES+) m/e (rel intensity) 419 (MH$^+$, 100); HRMS (ES+) calcd for $C_{20}H_{24}N_2O_4PS$ (MH$^+$) 419.1194, found 419.1203.

Diethyl 1-Oxo-4′-phenyl-1,2′,3,4′-tetrahydrospiro[indene-2,3′-pyrazole]-5′-ylphosphonate (13e): Yellow oil; yield method A 100 mg, 50%, method B 144 mg, 72%; IR (neat, cm^{-1}) 3233 (br, m), 2985 (m), 2930 (w), 1716 (s), 1606 (m), 1239 (s), 1026 (vs); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.12 (t, J = 6.9 Hz, 3H), 1.24 (t, J = 7.2 Hz, 3H), 2.94 (s, 2H), 3.83−3.91 (m, 1H), 3.92−4.12 (m, 3H), 4.43 (s, 1H), 6.65 (s, 1H), 7.11−7.14 (m, 2H), 7.24 (d, J = 7.5 Hz, 1H), 7.30−7.37 (m, 3H), 7.41 (t, J = 7.5 Hz, 1H), 7.58 (ddd collapsed to td, J = 7.5, 1.2 Hz, 1H), 7.79 (dd, J = 7.5, 1.2 Hz, 1H); ^{13}C ($CDCl_3$, 100 MHz) δ 16.1 (d, J_{C-P} = 6.7 Hz), 16.3 (d, J_{C-P} = 6.7 Hz), 35.0, 59.2 (d, J_{C-P} = 21.2 Hz), 62.7 (d, J_{C-P} = 5.4 Hz), 62.8 (d, J_{C-P} = 5.2 Hz), 77.0 (d, J_{C-P} = 4.6 Hz), 125.3, 126.4, 128.3, 128.4, 129.0, 129.1, 133.3, 135.5, 135.9, 147.1 (d, J = 227.0 Hz), 151.4, 203.4; ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$) δ 7.54; MS (ES+) m/e (rel intensity) 399 (MH$^+$, 100), 254 (15); HRMS (ES+) calcd for $C_{21}H_{24}N_2O_4P$ (MH$^+$) 399.1474, found 399.1454.

Diethyl 4′-(4-Chlorophenyl)-1-oxo-1,2′,3,4′-tetrahydrospiro-[indene-2,3′-pyrazole]-5′-ylphosphonate (13f): Yellow oil; yield method A 112 mg, 52%, method B 160 mg, 74%; IR (neat, cm^{-1}) 3235 (m), 2987 (m), 2931 (w), 2908 (w), 1716 (s), 1606 (m), 1240 (s), 1028 (s); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.17 (t, J = 7.2 Hz, 3H), 1.26 (t, J = 7.2 Hz, 3H), 2.93 (ABq, J = 17.6 Hz, 2H), 3.89−3.98 (m, 1H), 3.99−4.12 (m, 3H), 4.41 (s, 1H), 7.07 (d, J = 8.8 Hz, 2H), 7.26 (d, J = 7.5 Hz, 1H), 7.31 (d, J = 8.8 Hz, 2H), 7.42 (dd collapsed to t, J = 7.5 Hz, 1H), 7.59 (ddd collapsed to td, J = 7.5, 1.2 Hz, 1H), 7.79 (dd, J = 7.5, 1.2 Hz, 1H); ^{13}C ($CDCl_3$, 100 MHz) 16.1 (d, J_{C-P} = 6.7 Hz), 16.2 (d, J_{C-P} = 6.7 Hz), 34.8, 58.4 (d, J_{C-P} = 21.0 Hz), 62.8 (d, J_{C-P} = 5.0 Hz), 76.8, 125.2, 126.4, 128.4, 129.1, 130.4, 133.2, 134.08, 134.14, 136.0, 146.1 (d, J = 227.8 Hz), 151.2, 203.1; ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$) δ 7.37; MS (ES+) m/e (rel intensity) 435 ([M + 2]H$^+$), 433 (MH$^+$, 100); HRMS (ES+) calcd for $C_{21}H_{23}N_2O_4PCl$ (MH$^+$) 433.1084, found 433.1091.

■ ASSOCIATED CONTENT

Supporting Information. Complete characterization data for all the new compounds, X-ray data tables and CIF files for **5e** and **13c**, and copies of NMR spectra for all the new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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■ DEDICATION

§Dedicated to Prof. C. Chattopadhyay on the occasion of his 70th birthday.

■ REFERENCES

(1) (a) Elguero, J. In *Comprehensive Heterocyclic Chemistry*; Katritzky, A. R., Rees, C. W., Scriven, E. F. V., Eds.; Pergamon: Oxford, 1996; Vol. 3, p 1. For selected recent reviews, see: (b) Dolzhenko, A. V.; Dolzhenko, A. V.; Chui, W.-K. *Heterocycles* **2008**, *75*, 1575. (c) Lamberth, C. *Heterocycles* **2007**, *71*, 1467.

(2) For a recent review, see: Halcrow, M. A. *Dalton Trans.* **2009**, 2059.

(3) Balczewski, P.; Bodzioch, A. *Organophosphorus Chem.* **2009**, *38*, 279.

(4) Palacios, F.; Alonso, C.; de los Santos, J. M. *Chem. Rev.* **2005**, *105*, 899.

(5) For selected reviews, see: (a) Molteni, G. *ARKIVOC* **2007**, 224. (b) Regitz, M.; Heydt, H. In *1,3-Dipolar Cycloaddition Chemistry*; Padwa, A., Ed.; Wiley Interscience: New York, 1984; Chapter 4. (c) Zollinger, H. *Diazo Chemistry II-Aliphatic, Inorganic and Organometallic Compounds*; VCH: Weinheim, Germany, 1995; p 11. (d) Diederrich, F.; Isaacs, L.; Philip, D. *Chem. Soc. Rev.* **1994**, *23*, 243. (e) Trivedi, G. K. *J. Ind. Chem. Soc.* **2004**, *81*, 187.

(6) For a review, see: Kumar, V.; Aggarwal, R.; Singh, S. P. *Heterocycles* **2008**, *75*, 2893.

(7) (a) Ohira, S. *Synth. Commun.* **1989**, *19*, 561. (b) Mueller, S.; Liepold, B; Roth, G. J.; Bestmann, H. J. *Synlett* **1996**, 521. (c) The commercially available (Aldrich) 2-oxopropylphosphonate can be transformed in one step to **2**: Meffre, P.; Hermann, S.; Durand, P.; Reginato, G.; Riu, A. *Tetrahedron* **2002**, *58*, 5159.

(8) (a) Muruganantham, R.; Mobin, S. M.; Namboothiri, I. N. N. *Org. Lett.* **2007**, *9*, 1125. (b) Muruganantham, R.; Namboothiri, I. N. N. *J. Org. Chem.* **2010**, *75*, 2197.

(9) Mohanan, K.; Martin, A. R.; Toupet, L.; Smietana, M.; Vasseur, J. *Angew. Chem., Int. Ed.* **2010**, *49*, 3196.

(10) Xie, J.-W.; Wang, Z.; Yang, W.-J.; Kong, L.-C.; Xu, D.-C. *Org. Biomol. Chem.* **2009**, *7*, 4352.

(11) For recent reviews, see: (a) Zanatta, S. D. *Aust. J. Chem.* **2007**, *60*, 963. (b) Eymery, F.; Iorga, B.; Savignac, P. *Synthesis* **2000**, 185. For selected recent articles, see: (c) Baxendale, I. R.; Ley, S. V.; Mansfield, A. C.; Smith, C. D. *Angew. Chem., Int. Ed.* **2009**, *48*, 4017. (d) Stecko, S.; Mames, A.; Furman, B.; Chmielewski, M. *J. Org. Chem.* **2009**, *74*, 3094. (e) Souweha, M. S.; Enright, G. D.; Fallis, A. G. *Org. Lett.* **2007**, *9*, 5163. (f) Sahu, B.; Muruganantham, R.; Namboothiri, I. N. N. *Eur. J. Org. Chem.* **2007**, 2477. For a recent report on the application of the 2-phenyl analogue of **2** for the homologation of aldehydes to acetylenes, see: (g) Taber, D. F.; Bai, S.; Guo, P. *Tetrahedron Lett.* **2008**, *49*, 6904.

(12) Korgaokar, S. S.; Patil, P. H.; Shah, M. J; Parekh, H. H. *Ind. J. Pharm. Sci.* **1996**, *58*, 222.

(13) (a) Palaska, E.; Aytemir, M.; Uzbay, I. T.; Erol, D. *Eur. J. Med. Chem.* **2001**, *36*, 539. (b) Rajendra, P. Y.; Lakshmana, R. A.; Prasoona, L.; Murali, K.; Ravi, K. P. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 5030.

(14) Ozdemir, Z.; Kandilici, H. B.; Gumusel, B.; Calis, U.; Bilgin, A. A. *Eur. J. Med. Chem.* **2007**, *42*, 373–379.

(15) Udupi, R. H.; Kushnoor, A. S.; Bhat, A. R. *Ind. J. Heterocycl. Chem.* **1998**, *8*, 63.

(16) Nauduri, D.; Reddy, G. B. *Chem. Pharm. Bull.* **1998**, *46*, 1254.

(17) Taylor, E. C.; Patel, H. H. *Tetrahedron* **1992**, *48*, 8089.

(18) (a) Mustafa, A.; Hilmy, M. K. *J. Chem. Soc.* **1951**, 3254. (b) Fateen, A. K.; Ali, M. M. *Indian J. Chem.* **1972**, *10*, 968. (c) Tóth, G.; Lévai, A.; Szöllősy, Á.; Duddeck, H. *Tetrahedron* **1993**, *49*, 863. (d) Neudeck, H. K. *Monatsh. Chem.* **1996**, *127*, 417. (e) Lévai, A.; Silva, A. M. S.; Patonay, T.; Cavaleiro, J. A. S. *J. Heterocycl. Chem.* **1999**, *36*, 1215. (f) Lévai, A. *Org. Prep. Proced. Int.* **2002**, *34*, 425. (g) Azizian, J.; Shaabanzadeh, M.; Hatamjafari, F.; Mohammadizadeh, M. R. *ARKIVOC* **2006**, *xi*, 47. (h) Lévai, A.; Simon, A.; Jenei, A.; Kálmán, G.; Jekő, J.; Tóth, G. *ARKIVOC* **2009**, *xii*, 161.

(19) Molchanov, A. P.; Korotkov, V. S.; Kostikov, R. R. *Russ. J. Org. Chem.* **2004**, *40*, 470.

(20) Hassaneen, H. M.; Elwan, N.; Hassaneen, H. M. *Synth. Commun.* **2002**, *32*, 3047.

(21) Abdou, W. M.; Khidre, M. D.; Khidre, R. E. *Eur. J. Med. Chem.* **2009**, *44*, 526.

(22) Due to poor solubility and basicity of K_2CO_3 in EtOH, the active base NaOEt is generated very slowly in a controlled manner which appears beneficial in this case. See: Platonov, A. Y.; Evdokimov, A. N.; Kurzin, A. V.; Maiyorova, H. D. *J. Chem. Eng. Data* **2002**, *47*, 1175.

(23) Vogel's Text Book of *Practical Organic Chemistry*, 5th ed.; Addison Wesley Longman Ltd.: Essex, England, 1989; 1034 pp.

(24) (a) Xin, Y.; Zang, Z.-H.; Chen, F. L. *Synth. Commun.* **2009**, *39*, 4062. (b) Pinto, D. C. G. A.; Silva, A. M. S.; Lévai, A.; Cavaleiro, J. A. S.; Patonay, T.; Elguero, J. *Eur. J. Org. Chem.* **2000**, 2593.

(25) (a) Saxena, M. K.; Bokadia, M. M. J. *Ind. Chem. Soc.* **1969**, *46*, 855. (b) Saraf, S. D. *Can. J. Chem.* **1969**, *47*, 1169.

(26) Hallgas, B.; Dobos, Z.; Ősz, E.; Hollósy, F.; Schwab, R. E.; Szabó, E. Z.; Erős, D.; Idei, M.; Kéri, G.; Lórand, T. *J. Chromatogr. B* **2005**, *819*, 283.