Note

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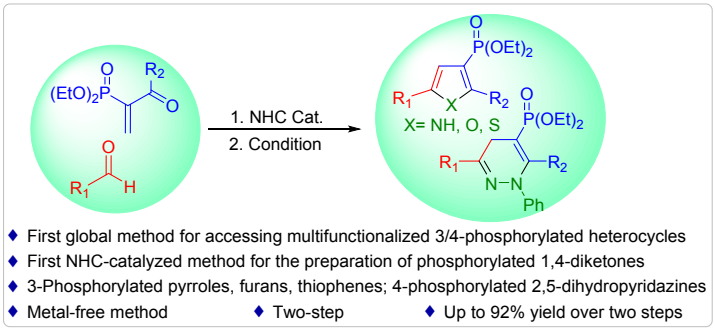


ABSTRACT: The first global method for the preparation of 3-phosphorylated-pyrroles, -furans, -thiophenes, and 4-phosphorylated 2,5-dihydropyridazines is reported. To achieve this, the first protocol for the direct synthesis of α-phosphorylated 1,4-diketones has been developed through a carbene-catalyzed Stetter reaction of vinylphosphonates and aldehydes. This is the first synthetic method for accessing 4-phosphorylated 2,5-dihydropyridazines. This process is metal-free and produces multi-functionalized heterocycles.

Phosphorylated aryls and heteroaryls have ubiquitous occurrence in pharmaceutics, agrochemicals, functionalized materials, organic synthesis as ligands and intermediates, and are closely related to life science.[1] They show unique bioactivities by virtue of P=O group acting as a strong hydrogen bond acceptor with proteins.[2] For heterocycles like pyrroles, furans and thiophenes, accessing 3/4-phosphorylated derivatives has remained challenging compared to 2-substituted analogs due to a lower reactivity of the C-3/4. Several valuable methods for their preparation have been developed. These methods generally rely on metal-catalyzed cyclization of phosphoryl-functionalized substrates, directing group-assisted functionalization or metal-catalyzed substitution in aryl halides. Some of the recent reports for the preparation of pyrroles include Steven's $ZnCl_2$-catalyzed cyclization of **A**, Deb's $PdCl_2/Cu(OAc)_2$-catalyzed cyclization of **B**, and Lopez's $IPr(CH_3CN)AuSbF_6$-catalyzed cyclization of **C** (Scheme 1).[3] The group of Jiang prepared furans using $(EtO)_2POH/Cs_2CO_3$ from **D**.[4] Hong, Yamaguchi and Muimo achieved phosphorylation of **E**, **F** and **G** using $[RhCp^*Cl_2]_2/AgNTf_2/Ag_2CO_3$, $Ni(OAc)_2$/dcypt and $Pd(OAc)_2$/dppf/$EtNiPr_2$/$(EtO)_2P(O)H$, respectively.[5] Despite the success, these methods suffer from one or multiple limitations like: (i) suitable for one specific class of

Scheme 1: Recent Approaches for the Preparation of 3-Phosphorylated Pyrroles, Furans and Thiophenes

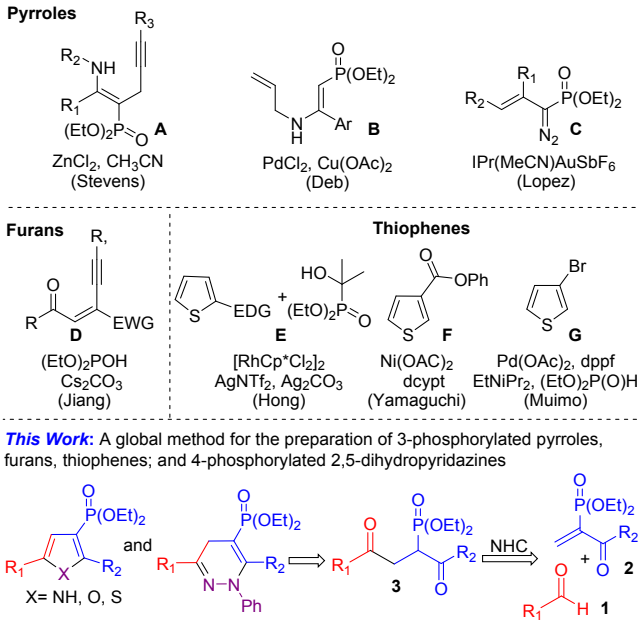
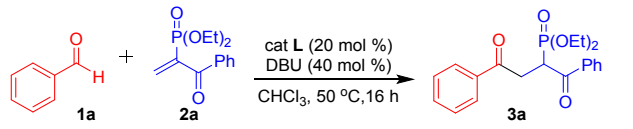
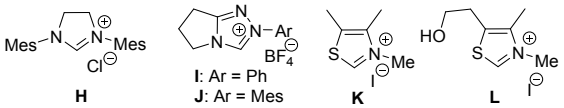


Table 1. Optimization of the Reaction Condition[a]



Entry	Deviation from the standard condition	Yield (%)[b]
1	no catalyst	0
2	**H** instead of **L**	48
3	**I** and **J** instead of **L**	trace
4	**K** instead of **L**	64
5	none	95
6	CH_2Cl_2 instead of $CHCl_3$	77
7	$(CH_2Cl)_2$ instead of $CHCl_3$	61
8	DABCO instead of DBU	21
9	^{t}BuOK instead of DBU	26
10	TMG instead of DBU	89
11	rt instead of 50 °C	67



[a]Standard reaction condition, unless otherwise specified: **1a** (0.15 mmol), **2a** (0.10 mmol), **L** (20 mol %), DBU (40 mol %), $CHCl_3$ (1.0 mL) at 50 °C for 16 h. [b]Isolated yield of **3a**. DBU=1,8-Diazabicycloundec-7-ene, DABCO=1,4-Diazabicyclo[2.2.2]octane, TMG=1,1,3,3-Tetramethylguanidine.

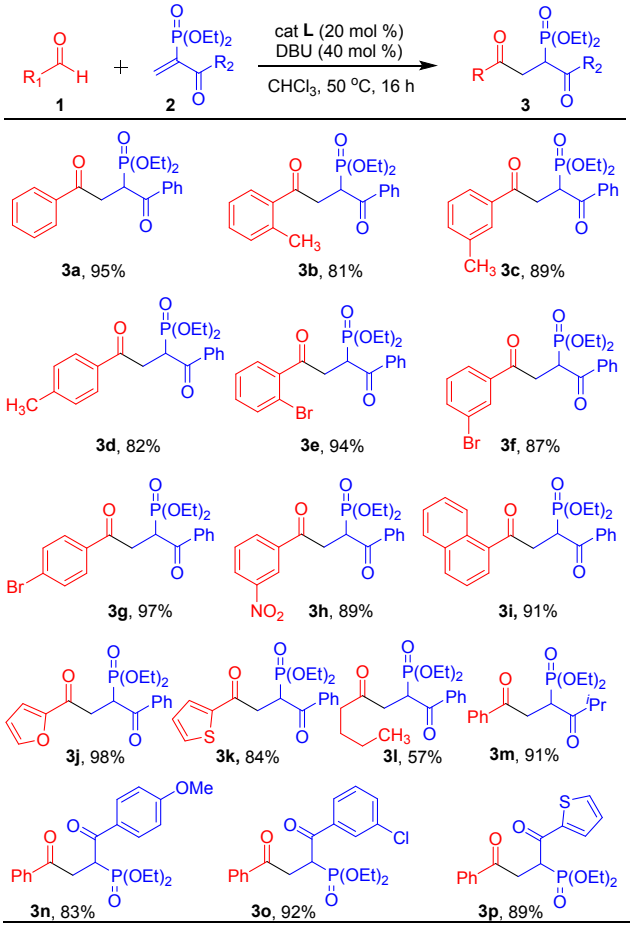
heterocycle, (ii) multistep preparation of complex advanced substrates, (iii) transition-metal catalyzed, and (iv) require directing group on the ring. To our knowledge, the literature is elusive of any general method suitable for the preparation of 3-phosphorylated-pyrroles, -furans, and -thiophenes. In addition, the synthesis of 4-phosphorylated 2,5-dihydropyridazines is yet to be achieved.

We hypothesized that all these challenging heterocycles could be obtained from a common *α*-phosphorylated 1,4-diketone intermediate **3** (Scheme 1). Our literature survey did not lead to any precedence, either metal- or organo-catalyzed, on the synthesis of **3**. Consequently, developing an effective synthetic method for **3**, possibly metal-free and organocatalytic, was key to the success of this study. With a long interest in metal-free catalysis, we were interested to develop the first *N*-heterocyclic harbene (NHC)-catalyzed method for the preparation of **3** through Stetter reaction of aldehyde **1** with vinylphosphonate **2**.[6,7]

Our study commenced using aldehyde **1a** and vinylphosphonate **2a**. The key results of reaction condition optimization are enlisted in Table 1. Precatalyst **H** in $CHCl_3$ in the presence of DBU base at 50 °C produced **3a** in 48% yield (entry 2). The *N*-Ph- as well as *N*-Mes-protected pyrrolidinone-based triazolium salts were not suitable for this reaction (**I** and **J**, entry 3). The use of thiazolium salt **K** improved the yield to 64% (entry 4). Switching to salt **L** gratifyingly produced **3a** in an excellent yield of 95% (entry 5). Screening of several other solvents and bases under a condition similar to entry 5 generated the desired product with a diminished yield (entries 6-10).

We next sought to examine the generality of this Stetter

Scheme 2. Scope of Aldehydes and Vinylphosphonates[a]



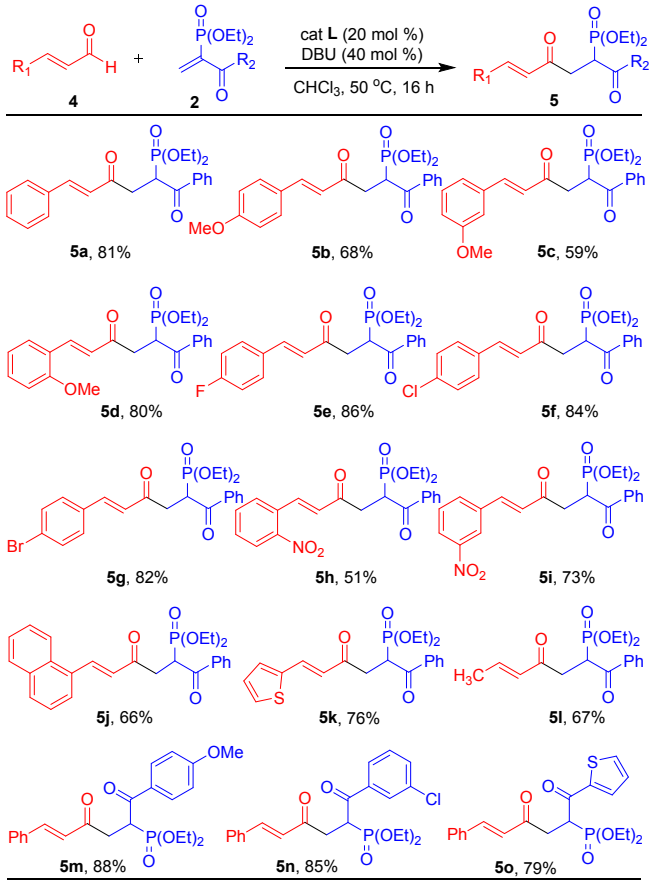
[a]Standard reaction condition as in entry 1, Table1. Yields are the isolated yields after column chromatography.

reaction using different aldehydes and vinylphosphonates under the standard condition. As demonstrated in Scheme 2, arylaldehydes substituted with electron-donating groups (EDG), such as methyl, at *ortho*, *meta* or *para*-position reacted well to give the desired product in 81-89% yield (**3b-3d**). Likewise, the electron-withdrawing groups (EWG) on arylaldehydes were well tolerated giving the diketones in 87-97% yield (**3e-3h**). The substitution pattern (*ortho*/*meta*/*para*) on the aryl rings did not show any general effect on the reactivity. Next, polyaromatic and heteroaromatic aldehydes were efficiently converted to produce **3i-3k** in excellent yields. Notably, an aliphatic aldehyde also reacted smoothly to afford the phosphorylated diketone **3l** in a descent yield. We next examined the substitution effect on vinylphosphonates **2** in reaction with **1a**. The reactions tolerated well aliphatic, both electron-rich as well as electron-deficient aryl, and heteroaryl-derived **2** to produce the desired products in excellent yields (**3m-3p**). *β*-phenyl-substituted vinylphosphonate (a derivative of **2a**) under this reaction condition remained largely unconsumed. Performing the reaction on 2.24 mmol scale (0.60 g) of vinylphosphonate **2a** produced the desired product **3a** in 91% isolated yield.

Further expanding the scope of the reaction, we used different enals **4** (Scheme 3). These α,β-unsaturated aldehydes have

remained comparatively challenging substrates for Stetter-type reaction due to a competing

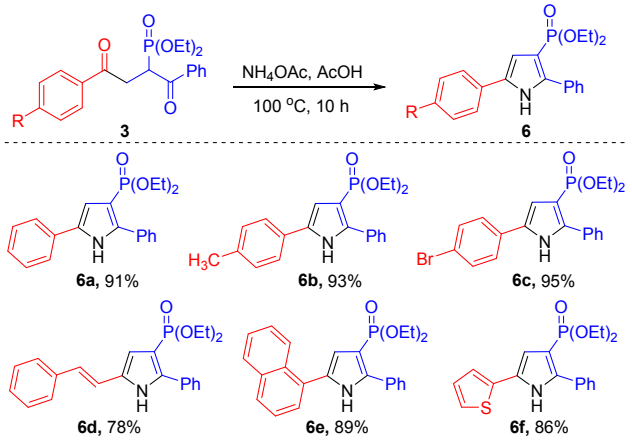
Scheme 3. Scope of Enals and Vinylphosphonates[a]



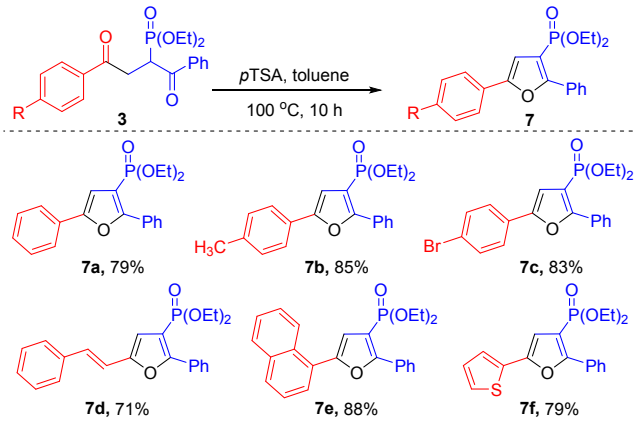
[a]Standard reaction condition as in entry 1, Table1. Yields are the isolated yields after column chromatography.

homoenolate and enolate reaction pathways. In general, both electron-deficient as well as electron-rich enals underwent this coupling reaction to afford the Stetter products in good to excellent yields (**5a-5i**). As in the case of aryl aldehydes, here also no generality on the reaction outcome among *ortho*, *meta* and *para*-substitution was observed. Polyaromatic and heteroaromatic enals were equally compatible under the optimized condition and gave the corresponding products in excellent yields (**5j-5k**).

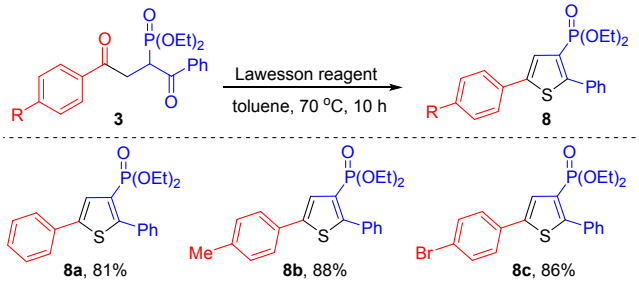
Scheme 4. Preparation of 3-Phosphorylated Pyrroles



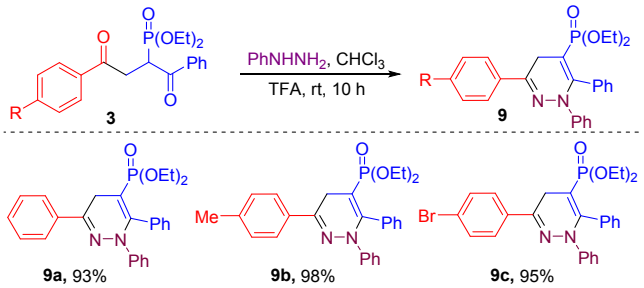
Scheme 5. Preparation of 3-Phosphorylated Furans



Scheme 6. Preparation of 3-Phosphorylated Thiophenes



Scheme 7. Preparation of 4-Phosphorylated 2,5-Dihydropyridazines



β-Methyl-substituted enal was also tolerated to produce **5l** in 67% yield. We next examined the scope of vinylphosphonates **2**. Electron-rich as well as –deficient aryl, and heteroaryl

substituted vinylphosphonates reacted well with **4a** to generate the desired products in 79-88% yield (**5m-5o**).

After successfully developing the catalytic method for the preparation of a wide range of *α*-phosphorylated 1,4-diketones, we next undertook the preparation of different class of 3/4-phosphorylated heterocycles. For all classes of heterocycles prepared here, such as 3-phosphorylated-pyrroles, -furans and thiophenes, and 4-phosphorylated 2,5-dihydropyridazines, we demonstrated the efficiency of our method using electron-rich, electron-deficient (hetero)aryl-substituted 1,4-diketones. The diketones **3a**, **3d**, **3g**, **3i**, **3k** and **5a** smoothly converted to 3-phosphorylated pyrroles **6a-6f** in the presence of NH_4OAc in AcOH at an elevated temperature in 78-95% yield (Scheme 4).[8] When this set of diketones were treated with *p*TSA in toluene, the 3-phosphorylated furans **7a-7f** were obtained in 71-88% yield (Scheme 5).[9] Upon subjecting **3a**, **3d** and **3g** with Lawesson's reagent in toluene at 70 °C, 3-phosphorylated thiophenes **8a-8c** were obtained in 81-88% yield (Scheme 6).[10] Finally, these diketones could be converted to 4-phosphorylated 2,5-dihydropyridazines **9a-9c** using $PhNHNH_2$ in excellent yields of 93-98% (Scheme 7).[11] The observed regioselectivity may be attributed to the steric hindrance from the phosphoryl group to the neighbouring carbonyl functionality.

In summary, we have developed the first general method for the preparation of highly functionalised 3-phosphorylated-pyrroles, -furans and -thiophenes; and 4-phosphorylated 2,5-dihydropyridazines from vinylphosphonates and aldehydes. To achieve this, the first NHC-catalyzed Stetter reaction was developed for the preparation of *α*-phosphorylated-1,4-diketones for a wide range of aldehydes, enals and vinylphosphonates. This is the first method to synthesize 4-phosphorylated 2,5-dihydropyridazines. This two-step method is metal-free and highly efficient. This study is expected to further augment the bioactivity evaluation of different class of phosphorylated heterocycles.

EXPERIMENTAL SECTION

General Information: Aldehydes and other reagents were purchased from a commercial supplier and used without further purification. All reactions were performed in oven-dried glasswares. The *α,β*-unsaturated aldehydes **4** and vinylphosphonates **2** were prepared following literature known methods.[12,13] Solvents were dried and distilled following the standard procedures; TLC was carried out on pre-coated plates (Merck silica gel 60, f_{254}), and the spots were visualized with UV light or by charring the plates dipped in PMA charring solution. Flash chromatography was performed using silica gel (230-400 mess) with distilled solvents. ^1H, ^{13}C and ^{31}P NMR for compounds were recorded at 400 MHz, 100 MHz and 162 MHz instrument respectively using $CDCl_3$ as the solvent. 98% PPh_3 was used as an external standard for ^{31}P NMR. Chemical shifts were recorded in parts per million (ppm, δ) relative to tetramethylsilane (δ 0.00). ^1H NMR splitting patterns are designated as singlet (s), doublet (d), triplet (t), quartet (q), dd (doublet of doublets); m (multiplets), etc. High-resolution mass spectral analysis (HRMS) was performed on Q-TOF Premier mass spectrometer. The melting points were recorded on Buchi M-560 melting point apparatus and are uncorrected.

General procedure for the NHC-Catalyzed Synthesis of 3 and 5: To an oven-dried Schlenk tube equipped with a magnetic stir bar, was added aldehyde **1** or **4** (0.15 mmol, 1.5 equiv.), vinylphosphonate **2** (0.1 mmol, 1.0 equiv.) and catalyst **L** (20 mol %) in $CHCl_3$ (1.0 mL) at room temperature. The reaction chamber was purged with argon and DBU (40 mol %) was added. After stirring this reaction mixture at 50 °C in an oil bath for 16 h, the solvent was evaporated under the reduced pressure. The crude mass was purified by flash column chromatography on silica gel using 60% EtOAc in hexane to obtain the pure desired products **3** or **5**.

*The preparation of **3a** on gram scale:* The product **3a** was obtained in 91% yield (0.76 g) when the reaction was run using **1a** (0.356 g, 3.36 mmol) and **2a** (0.60 g, 2.24 mmol) under the optimized reaction condition.

General procedure for the synthesis of compounds 6, 7, 8 and 9:

Pyrroles 6: To an oven-dried sealed tube equipped with a magnetic stir bar, was added ketophosphonates **3** or **5** (0.10 mmol), NH_4OAc (0.115 g, 1.50 mmol) in AcOH (1.0 mL) and the reaction chamber was sealed. After stirring at 100 °C in an oil bath for 10 h, the reaction mixture was quenched with a saturated aqueous solution of $NaHCO_3$, extracted with CH_2Cl_2 (2 x 10 ml). The combined organic layers were dried over anhydrous Na_2SO_4, evaporated under reduced pressure and the crude product was purified by flash column chromatography on silica gel using 60% EtOAc in hexane to obtain the pure desired product **6**.

Furans 7: To an oven-dried sealed tube equipped with a magnetic stir bar, ketophosphonates **3** or **5** (0.10 mmol), *p*-TSA (0.028 g, 0.15 mmol) and toluene (1.0 mL) was added and the reaction chamber was sealed. After stirring the reaction mixture at 100 °C in an oil bath for 10 h, the solvent was evaporated under a reduced pressure and the compound was purified by flash column chromatography on silica gel using 60% EtOAc in hexane to obtain the pure desired product 7.

Thiophenes 8: To an oven-dried sealed tube equipped with a magnetic stir bar, was added ketophosphonates **3** (0.10 mmol), Lawesson's reagent (0.048 g, 0.12 mmol) and toluene (1.0 mL) and the reaction chamber was sealed. After being stirred at 70 °C in an oil bath for 10 h, the reaction mixture was cooled to room temperature and the solvent was evaporated under a reduced pressure. The crude product was purified by flash column chromatography on silica gel using 60% EtOAc in hexane to obtain the pure furans **8**.

2,5-Dihydropyridazines 9: To an oven-dried sealed tube equipped with a magnetic stir bar, was added ketophosphonates **3** (0.10 mmol), $PhNHNH_2$ (17.8 µL, 0.15 mmol), $CHCl_3$ (1.0 mL) and TFA (10.0 µL, 0.13 mmol) was added, and the reaction chamber was sealed. After stirring the reaction mixture for 10 h at room temperature, the solvent was evaporated under a reduced pressure. The crude product was purified by flash column chromatography on silica gel using 60% EtOAc in hexane to obtain the pure desired product **9**.

Characterization of the products:

Diethyl (1,4-dioxo-1,4-diphenylbutan-2-yl)phosphonate (**3a**): 95% yield (36 mg), pale yellow gummy liquid, eluent: 60% EtOAc in hexane. ^1H NMR (400 MHz, $CDCl_3$): δ 1.08 (3H, t, J = 6.8 Hz), 1.17 (3H, t, J = 6.8 Hz), 3.47-3.64 (1H, m), 3.85-4.22 (5H, m), 4.63-4.87 (1H, m), 7.28-7.56 (6H, m), 7.91 (2H, d, J = 7.2 Hz), 8.04 (2H, d, J = 7.6 Hz); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 16.1 (q, $J_{C\text{-}P}$ = 7.0 Hz), 37.3 (d, $J_{C\text{-}P}$ = 1 Hz), 42.3 (d,

$J_{C\text{-}P}$ = 128.0 Hz), 62.9 (t, $J_{C\text{-}P}$ = 7.0 Hz), 128.2, 128.4, 128.6, 128.9, 133.2, 133.5, 135.9, 137.4, 195.2 (d, $J_{C\text{-}P}$ = 5.0 Hz), 196.6 (d, $J_{C\text{-}P}$ = 15.0 Hz); $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$): δ 22.3; HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd. for $C_{20}H_{23}O_5PNa^+$ 397.1176, found: 397.1171.

Diethyl (1,4-dioxo-1-phenyl-4-(o-tolyl)butan-2-yl)phosphonate (**3b**): 81% yield (32 mg), pale yellow gummy liquid, eluent: 60% EtOAc in hexane. ^1H NMR (400 MHz, $CDCl_3$): δ 1.07 (3H, t, J = 7.2 Hz), 1.16 (3H, t, J = 6.8 Hz), 2.34 (3H, s), 3.33-3.35 (1H, m), 3.85-4.16 (5H, m), 4.61-4.84 (1H, m), 7.10-7.26 (2H, m), 7.30 (1H, t, J = 7.2 Hz), 7.41 (2H, t, J = 7.6 Hz), 7.50 (1H, t, J = 7.2 Hz), 7.74 (1H, d, J = 7.6 Hz), 8.04 (2H, d, J = 7.2 Hz); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 16.1 (q, $J_{C\text{-}P}$ = 6.0 Hz), 21.3, 39.6 (q, $J_{C\text{-}P}$ = 1.0 Hz), 42.7 (d, $J_{C\text{-}P}$ = 127.0 Hz), 62.8 (t, $J_{C\text{-}P}$ = 7.0 Hz), 125.7, 128.4, 128.9, 128.9, 131.7, 131.9, 133.2, 136.6, 137.4, 138.5, 195.3 (d, $J_{C\text{-}P}$ = 4.0 Hz), 200.1 (d, $J_{C\text{-}P}$ = 16.0 Hz); $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$): δ 22.3; HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd. for $C_{21}H_{25}O_5PNa^+$ $[M+Na]^+$: 411.1332, found: 411.1329.

Diethyl (1,4-dioxo-1-phenyl-4-(m-tolyl)butan-2-yl)phosphonate (**3c**): 89% yield (35 mg), pale yellow gummy liquid, eluent: 60% EtOAc in hexane. ^1H NMR (400 MHz, $CDCl_3$): δ 1.09 (3H, t, J = 7.2 Hz), 1.16 (3H, t, J = 7.2 Hz), 2.32 (3H, s), 3.44-3.62 (1H, m), 3.88-4.20 (5H, m), 4.62-4.82 (1H, m), 7.22-7.35 (2H, m), 7.41 (2H, t, J = 7.2 Hz), 7.50 (1H, t, J = 7.6 Hz), 7.71 (2H, d, J = 6.4 Hz), 8.04 (2H, t, J = 7.2 Hz); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 16.1 (q, $J_{C\text{-}P}$ = 6.0 Hz), 21.2, 37.3, 42.4 (d, $J_{C\text{-}P}$ = 128.0 Hz), 62.8 (t, $J_{C\text{-}P}$ = 8.0 Hz), 125.4, 128.4, 128.5, 128.8, 128.9, 133.1, 134.2, 135.9, 137.4, 138.4, 195.3 (d, $J_{C\text{-}P}$ = 5.0 Hz), 196.7 (d, $J_{C\text{-}P}$ = 16.0 Hz); $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$): δ 22.3; HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd. for $C_{21}H_{25}O_5PNa^+$ $[M+Na]^+$: 411.1332, found: 411.1328.

Diethyl (1,4-dioxo-1-phenyl-4-(p-tolyl)butan-2-yl)phosphonate (**3d**): 82% yield (32 mg), pale yellow gummy liquid, eluent: 60% EtOAc in hexane. ^1H NMR (400 MHz, $CDCl_3$): δ 1.08 (3H, t, J = 7.2 Hz), 1.17 (3H, t, J = 6.8 Hz), 2.33 (3H, s), 3.42-3.62 (1H, m), 3.87-4.17 (5H, m), 4.60-4.83 (1H, m), 7.18 (2H, d, J = 8.4 Hz), 7.41 (2H, t, J = 7.6 Hz), 7.50 (1H, t, J = 7.2 Hz), 7.81 (2H, d, J = 8.4 Hz), 8.04 (2H, t, J = 7.2 Hz); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 16.1 (q, $J_{C\text{-}P}$ = 6.0 Hz), 21.7, 37.2, 42.3 (d, $J_{C\text{-}P}$ = 128.0 Hz), 62.8 (t, $J_{C\text{-}P}$ = 7.0 Hz), 128.4, 128.5, 128.9, 129.3, 133.1, 133.5, 137.5, 144.4, 195.3 (d, $J_{C\text{-}P}$ = 5.0 Hz), 196.2 (d, $J_{C\text{-}P}$ = 16.0 Hz); $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$): δ 22.4; HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd. for $C_{21}H_{25}O_5PNa^+$ $[M+Na]^+$: 411.1332, found: 411.1330.

Diethyl (4-(2-bromophenyl)-1,4-dioxo-1-phenylbutan-2-yl)phosphonate (**3e**): 94% yield (43 mg), pale yellow gummy liquid, eluent: 60% EtOAc in hexane. ^1H NMR (400 MHz, $CDCl_3$): δ 1.08 (3H, t, J = 6.8 Hz), 1.15 (3H, t, J = 6.8 Hz), 3.38-3.53 (1H, m), 3.86-4.09 (5H, m), 4.61-4.83 (1H, m), 7.15-7.36 (2H, m), 7.37-7.59 (5H, m), 8.02 (2H, d, J = 7.6 Hz); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 16.1 (q, $J_{C\text{-}P}$ = 7.0 Hz), 37.2, 42.3 (d, $J_{C\text{-}P}$ = 128.0 Hz), 62.8 (t, $J_{C\text{-}P}$ = 6.0 Hz), 128.4, 128.7, 128.9, 129.7, 131.9, 133.2, 134.6, 137.2, 195.1 (d, $J_{C\text{-}P}$ = 5.0 Hz), 195.6 (d, $J_{C\text{-}P}$ = 16.0 Hz); $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$): δ 21.9; HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd. for $C_{20}H_{22}BrO_5PNa^+$ $[M+Na]^+$: 475.0281, found: 475.0274.

Diethyl (4-(3-bromophenyl)-1,4-dioxo-1-phenylbutan-2-yl)phosphonate (**3f**): 87% yield (40 mg), pale yellow gummy liquid, eluent: 60% EtOAc in hexane. ^1H NMR (400 MHz, $CDCl_3$): δ 1.09 (3H, t, J = 6.8 Hz), 1.16 (3H, t, J = 7.2 Hz), 3.39-3.57 (1H, m), 3.89-4.16 (5H, m), 4.61-4.79 (1H, m), 7.25 (1H, t, J = 8.0 Hz), 7.41 (2H, t, J = 7.6 Hz), 7.51 (1H, t, J = 7.2 Hz), 7.62 (1H, d, J = 8.0 Hz), 7.83 (1H, d, J = 7.6 Hz), 8.02 (3H, t, J = 5.6 Hz); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 16.1 (q, $J_{C\text{-}P}$ = 6.0 Hz), 37.3, 42.4 (d, $J_{C\text{-}P}$ = 128.0 Hz), 62.8 (t, $J_{C\text{-}P}$ = 6.0 Hz), 122.9, 126.7, 128.4, 128.9, 130.2, 131.2, 133.2, 136.3, 137.3, 137.6, 195.0 (d, $J_{C\text{-}P}$ = 5.0 Hz), 195.3 (d, $J_{C\text{-}P}$ = 16.0 Hz); $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$): δ 21.8; HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd. for $C_{20}H_{22}BrO_5PNa^+$ $[M+Na]^+$: 475.0281, found: 475.0276.

Diethyl (4-(4-bromophenyl)-1,4-dioxo-1-phenylbutan-2-yl)phosphonate (**3g**): 97% yield (45 mg), pale yellow gummy liquid, eluent: 60% EtOAc in hexane. ^1H NMR (400 MHz, $CDCl_3$): δ 1.08 (3H, t, J = 7.2 Hz), 1.16 (3H, t, J = 7.2 Hz), 3.42-3.55 (1H, m), 3.88-4.15 (5H, m), 4.60-4.80 (1H, m), 7.41 (2H, t, J = 7.2 Hz), 7.50 (3H, t, J = 7.2 Hz), 7.77 (2H, d, J = 8.4 Hz), 8.02 (2H, d, J = 7.2 Hz); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 16.1 (q, $J_{C\text{-}P}$ = 6.0 Hz), 37.2, 42.3 (d, $J_{C\text{-}P}$ = 128.0 Hz), 62.9 (q, $J_{C\text{-}P}$ = 6.0 Hz), 128.4, 128.7, 128.9, 129.7, 131.9, 133.2, 134.5, 137.2, 195.1 (d, $J_{C\text{-}P}$ = 5.0 Hz), 200.1 (d, $J_{C\text{-}P}$ = 16.0 Hz); $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$): δ 21.5; HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd. for $C_{20}H_{22}BrO_5PNa^+$ $[M+Na]^+$: 475.0281, found: 475.0278.

Diethyl (4-(3-nitrophenyl)-1,4-dioxo-1-phenylbutan-2-yl)phosphonate (**3h**): 89% yield (38 mg), pale yellow gummy liquid, eluent: 60% EtOAc in hexane. ^1H NMR (400 MHz, $CDCl_3$): δ 1.10 (3H, t, J = 7.2 Hz), 1.17 (3H, t, J = 7.2 Hz), 3.48-3.63 (1H, m), 3.90-4.08 (4H, m), 4.08-4.21 (1H, m), 4.65-4.82 (1H, m), 7.43 (2H, t, J = 7.2 Hz), 7.53 (1H, t, J = 7.6 Hz), 7.60 (1H, t, J = 8.0 Hz), 8.03 (2H, t, J = 7.2 Hz), 8.23 (1H, d, J = 8.0 Hz), 8.35 (1H, dd, J = 1.2 Hz), 8.74 (1H, t, J = 1.6 Hz); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 16.1 (q, $J_{C\text{-}P}$ = 3.0 Hz), 37.5, 42.5 (d, $J_{C\text{-}P}$ = 129.0 Hz), 63.1 (t, $J_{C\text{-}P}$ = 3.0 Hz), 123.2, 127.8, 128.5, 128.9, 130.0, 133.5, 133.8, 137.2, 148.5, 194.8 (d, $J_{C\text{-}P}$ = 6.0 Hz), 195.0 (d, $J_{C\text{-}P}$ = 5.0 Hz); $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$): δ 21.5; HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd. for $C_{20}H_{22}NO_7PNa^+$ $[M+Na]^+$: 442.1027, found: 442.1029.

Diethyl (4-(naphthalen-1-yl)-1,4-dioxo-1-phenylbutan-2-yl)phosphonate (**3i**): 91% yield (39 mg), pale yellow gummy liquid, eluent: 60% EtOAc in hexane. ^1H NMR (400 MHz, $CDCl_3$): δ 1.08 (3H, t, J = 7.2 Hz), 1.16 (3H, t, J = 6.8 Hz), 3.49-3.67 (1H, m), 3.91-4.09 (4H, m), 4.14-4.27 (1H, m), 4.76-4.92 (1H, m), 7.38-7.48 (5H, m), 7.51 (1H, t, J = 7.2 Hz), 7.77 (1H, d, J = 7.2 Hz), 7.92 (1H, d, J = 8.0 Hz), 7.99 (1H, d, J = 4.0 Hz), 8.08 (1H, d, J = 7.6 Hz), 8.45 (2H, d, J = 8.4 Hz); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 16.1 (q, $J_{C\text{-}P}$ = 7.0 Hz), 40.1, 42.9 (d, $J_{C\text{-}P}$ = 128.0 Hz), 62.8 (t, $J_{C\text{-}P}$ = 6.0 Hz), 124.3, 125.7, 126.4, 128.0, 128.3, 128.3, 128.4, 128.9, 130.1, 133.1, 133.2, 133.8, 134.3, 137.5, 195.4 (d, $J_{C\text{-}P}$ = 4.0 Hz), 200.3 (d, $J_{C\text{-}P}$ = 16.0 Hz); $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$): δ 22.2; HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd. for $C_{24}H_{25}O_5PNa^+$ $[M+Na]^+$: 447.1332, found: 447.1335.

Diethyl (4-(furan-2-yl)-1,4-dioxo-1-phenylbutan-2-yl)phosphonate (**3j**): 98% yield (36 mg), pale yellow gummy liquid, eluent: 60% EtOAc in hexane. ^1H NMR (400 MHz, $CDCl_3$): δ 1.08 (3H, t, J = 7.2 Hz), 1.16 (3H, t, J = 7.2 Hz), 3.31-3.48 (1H, m), 3.87-4.12 (5H, m), 4.59-4.79 (1H, m), 6.45 (1H, t, J = 1.6 Hz), 7.15 (1H, d, J = 3.6 Hz), 7.39 (2H, t, J = 7.6 Hz), 7.49 (2H, t, J = 7.2 Hz), 8.01 (2H, d, J = 8.0 Hz); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 16.1 (q, $J_{C\text{-}P}$ = 6.0 Hz), 36.7 (q, $J_{C\text{-}P}$ = 2.0 Hz), 41.9 (d, $J_{C\text{-}P}$ = 128.0 Hz), 62.8 (t, $J_{C\text{-}P}$ = 4.0 Hz), 112.3, 117.6, 128.4, 128.9, 133.2, 137.3, 146.6, 151.9, 185.7 (d, $J_{C\text{-}P}$ = 16.0 Hz), 195.2 (d, $J_{C\text{-}P}$ = 5.0 Hz); $^{31}P\{^1H\}$ NMR (162

MHz, $CDCl_3$): δ 21.8; HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd. for $C_{18}H_{21}O_6PNa^+$ $[M+Na]^+$: 387.0968, found: 387.0970.

Diethyl (1,4-dioxo-1-phenyl-4-(thiophen-2-yl)butan-2-yl)phosphonate (**3k**): 84% yield (32 mg), pale yellow gummy liquid, eluent: 60% EtOAc in hexane. ^1H NMR (400 MHz, $CDCl_3$): δ 1.09 (3H, t, J = 6.8 Hz), 1.16 (3H, t, J = 7.2 Hz), 3.41-3.57 (1H, m), 3.89-4.14 (5H, m), 4.64-4.81 (1H, m), 7.06 (1H, t, J = 4.4 Hz), 7.40 (2H, t, J = 7.6 Hz), 7.49 (1H, t, J = 7.2 Hz), 7.57 (1H, d, J = 4.8 Hz), 7.76 (1H, d, J = 4.0 Hz), 8.01 (2H, d, J = 7.6 Hz); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 16.1 (q, J_{C-P} = 6.0 Hz), 37.5 (d, J_{C-P} = 1.0 Hz), 42.3 (d, J_{C-P} = 128.0 Hz), 62.8 (t, J_{C-P} = 6.0 Hz), 128.2, 128.4, 128.9, 132.6, 133.2, 134.1, 137.3, 142.7, 189.5 (d, J_{C-P} = 17.0 Hz), 195.1 (d, J_{C-P} = 5.0 Hz); $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$): δ 21.8; HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd. for $C_{18}H_{21}O_5PSNa^+$ $[M+Na]^+$: 403.0740, found: 403.0743.

Diethyl (1,4-dioxo-1-phenyloctan-2-yl)phosphonate (**3l**): 57% yield (20 mg), pale yellow gummy liquid, eluent: 60% EtOAc in hexane. ^1H NMR (400 MHz, $CDCl_3$): δ 0.80 (3H, t, J = 7.2 Hz), 1.05 (3H, t, J = 6.8 Hz), 1.13-1.27 (5H, m), 1.40-1.52 (2H, m), 2.33-2.46 (2H, m), 2.84-3.03 (1H, m), 3.44-3.59 (1H, m), 3.86-4.08 (4H, m), 4.46-4.62 (1H, m), 7.39 (2H, t, J = 7.6 Hz), 7.49 (1H, t, J = 7.2 Hz), 7.96 (2H, d, J = 8.0 Hz); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 13.8, 16.1 (q, J_{C-P} = 6.0 Hz), 22.2, 25.7, 40.5 (d, J_{C-P} = 2.0 Hz), 41.6, 42.2 (d, J_{C-P} = 128.0 Hz), 62.7 (q, J_{C-P} = 6.0 Hz), 128.0, 128.4, 128.7, 128.9, 133.2, 137.4, 195.4 (d, J_{C-P} = 5.0 Hz), 207.6 (d, J_{C-P} = 16.0 Hz); $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$): δ 22.1; HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd. for $C_{18}H_{27}O_5PNa^+$ $[M+Na]^+$: 377.1489, found: 377.1492.

Diethyl (5-methyl-1,4-dioxo-1-phenylhexan-3-yl)phosphonate (**3m**): 91% yield (31 mg), colorless gummy liquid, eluent: 60% EtOAc in hexane. ^1H NMR (400 MHz, $CDCl_3$): δ 1.13 (3H, d, J = 6.8 Hz), 1.27-1.40 (9H, m), 3.13-3.38 (2H, m), 3.87-4.03 (1H, m), 4.04-4.24 (5H, m), 7.45 (2H, t, J = 8.0 Hz), 7.56 (1H, t, J = 7.2 Hz), 7.98 (2H, d, J = 7.6 Hz); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 16.3 (q, J_{C-P} = 5.0 Hz), 17.6, 19.5, 35.7 (d, J_{C-P} = 1.0 Hz), 41.4, 45.7 (d, J_{C-P} = 126.0 Hz), 62.7 (dd, J_{C-P} = 6.0 Hz, 7.0 Hz), 128.1, 128.5, 133.3, 136.1, 196.6 (d, J_{C-P} = 16.0 Hz), 208.8 (d, J_{C-P} = 4.0 Hz); $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$): δ 22.8; HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd. for $C_{17}H_{25}O_5PH^+$ $[M+H]^+$: 341.1513, found: 341.1511.

Diethyl (1-(4-methoxyphenyl)-1,4-dioxo-4-phenylbutan-2-yl)phosphonate (**3n**): 83% yield (34 mg), pale yellow gummy liquid, eluent: 60% EtOAc in hexane. ^1H NMR (400 MHz, $CDCl_3$): δ 1.21 (3H, t, J = 7.2 Hz), 1.26 (3H, t, J = 6.8 Hz), 3.52-3.65 (1H, m), 3.89 (3H, s), 3.98-4.27 (5H, m), 4.69-4.85 (1H, m), 6.98 (2H, d, J = 8.8 Hz), 7.45 (2H, t, J = 7.6 Hz), 7.57 (1H, t, J = 7.6 Hz), 8.0 (2H, d, J = 8.0 Hz), 8.12 (2H, d, J = 8.8 Hz); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 16.2 (t, J_{C-P} = 6.0 Hz), 37.2, 41.8 (d, J_{C-P} = 128.0 Hz), 55.5, 62.8 (q, J_{C-P} = 7.0 Hz), 113.6, 128.2, 128.6, 130.2, 133.4, 133.5, 135.9, 163.7, 193.3 (d, J_{C-P} = 5.0 Hz), 196.7 (d, J_{C-P} = 16.0 Hz); $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$): δ 22.7; HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd. for $C_{21}H_{25}O_5PNa^+$ $[M+Na]^+$: 427.1281, found: 427.1267.

Diethyl (1-(3-chlorophenyl)-1,4-dioxo-4-phenylbutan-2-yl)phosphonate (**3o**): 92% yield (37 mg), pale yellow gummy liquid, eluent: 60% EtOAc in hexane. ^1H NMR (400 MHz, $CDCl_3$): δ 1.20 (3H, t, J = 6.8 Hz), 1.27 (3H, t, J = 7.2 Hz), 3.56-3.70 (1H, m), 4.01-4.23 (5H, m), 4.60-4.79 (1H, m), 7.41-7.51 (3H, m), 7.54-7.62 (2H, m), 7.94-8.05 (2H, m), 8.07 (1H, s); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 16.1 (q, J_{C-P} = 7.0 Hz), 37.4, 42.7 (d, J_{C-P} = 128.0 Hz), 63.0 (d, J_{C-P} = 7.0 Hz), 127.1, 128.2, 128.7, 128.9, 129.7, 133.0, 133.6, 134.7, 135.7, 138.9, 194.2 (d, J_{C-P} = 6.0 Hz), 196.5 (d, J_{C-P} = 16.0 Hz); $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$): δ 21.7; HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd. for $C_{20}H_{22}ClO_5PNa^+$ $[M+Na]^+$: 431.0786, found: 431.0786.

Diethyl (1,4-dioxo-4-phenyl-1-(thiophen-2-yl)butan-2-yl)phosphonate (**3p**): 89% yield (33 mg), pale yellow gummy liquid, eluent: 60% EtOAc in hexane. ^1H NMR (400 MHz, $CDCl_3$): δ 1.21-1.31 (6H, m), 3.51-3.66 (1H, m), 4.05-4.22 (5H, m), 4.53-4.67 (1H, m), 7.19 (1H, t, J = 4.4 Hz), 7.45 (1H, d, J = 7.6 Hz), 7.57 (1H, t, J = 7.6 Hz), 7.69 (1H, d, J = 5.2 Hz), 7.99 (3H, t, J = 8.0 Hz); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 16.2 (t, J_{C-P} = 6.0 Hz), 36.8 (d, J_{C-P} = 2.0 Hz), 43.9 (d, J_{C-P} = 127.0 Hz), 62.9 (t, J_{C-P} = 7.0 Hz), 128.1, 128.2, 128.6, 133.5, 133.6, 134.4, 135.8, 144.0, 187.1 (d, J_{C-P} = 5.0 Hz), 196.4 (d, J_{C-P} = 15.0 Hz); $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$): δ 21.9; HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd. for $C_{18}H_{21}O_5PNa^+$ $[M+Na]^+$: 403.0740, found: 403.0739.

Diethyl (E)-(1,4-dioxo-1,6-diphenylhex-5-en-2-yl)phosphonate (**5a**): 81% yield (33 mg), pale yellow gummy liquid, eluent: 60% EtOAc in hexane. ^1H NMR (400 MHz, $CDCl_3$): δ 1.16 (3H, t, J = 6.8 Hz), 1.24 (3H, t, J = 6.8 Hz), 3.23-3.41 (1H, m), 3.78-3.96 (1H, m), 3.97-4.18 (4H, m), 4.63-4.86 (1H, m), 6.74 (1H, d, J = 16.4 Hz), 7.33-7.44 (3H, m), 7.45-7.67 (6H, m), 8.09 (2H, d, J = 7.6 Hz); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 16.0 (q, J_{C-P} = 6.0 Hz), 38.8, 42.2 (d, J_{C-P} = 128.0 Hz), 62.7 (t, J_{C-P} = 8.0 Hz), 124.9, 128.2, 128.3, 128.8, 128.9, 130.6, 133.1, 134.1, 137.3, 143.6, 195.2 (d, J_{C-P} = 5.0 Hz), 196.2 (d, J_{C-P} = 16.0 Hz); $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$): δ 22.2; HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd. for $C_{22}H_{25}O_5P$ Na^+ $[M+Na]^+$: 423.1332, found: 423.1329.

Diethyl (E)-(6-(4-methoxyphenyl)-1,4-dioxo-1-phenylhex-5-en-2-yl)phosphonate (**5b**): 68% yield (30 mg), pale yellow gummy liquid, eluent: 60% EtOAc in hexane. ^1H NMR (400 MHz, $CDCl_3$): δ 1.09 (3H, t, J = 7.2 Hz), 1.17 (3H, t, J = 6.8 Hz), 3.16-3.28 (1H, m), 3.71-3.84 (1H, m), 3.77 (3H, s), 3.91-4.08 (4H, m), 4.58-4.73 (1H, m), 6.56 (1H, d, J = 16.0 Hz), 6.84 (2H, d, J = 8.8 Hz), 7.41 (4H, t, J = 7.2 Hz), 7.50 (2H, t, J = 6.0 Hz), 8.02 (2H, d, J = 7.2 Hz); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 16.1 (q, J_{C-P} = 6.0 Hz), 38.8, 42.3 (d, J_{C-P} = 128.0 Hz), 55.4, 62.8 (t, J_{C-P} = 9.0 Hz), 114.4, 122.9, 126.9, 128.4, 128.9, 130.1, 133.1, 137.5, 143.5, 161.8, 195.4 (d, J_{C-P} = 5.0 Hz), 196.2 (d, J_{C-P} = 15.0 Hz); $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$): δ 22.4; HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd. for $C_{23}H_{27}O_6PNa^+$ $[M+Na]^+$: 453.1437, found: 453.1434.

Diethyl (E)-(6-(3-methoxyphenyl)-1,4-dioxo-1-phenylhex-5-en-2-yl)phosphonate (**5c**): 59% yield (25 mg), pale yellow gummy liquid, eluent: 60% EtOAc in hexane. ^1H NMR (400 MHz, $CDCl_3$): δ 1.09 (3H, t, J = 6.8 Hz), 1.16 (3H, t, J = 7.2 Hz), 3.16-3.32 (1H, m), 3.76 (3H, s), 3.72-3.88 (1H, m), 3.90-4.10 (4H, m), 4.58-4.74 (1H, m), 6.65 (1H, d, J = 16.0 Hz), 6.87 (1H, dd, J = 8 Hz), 6.98 (1H, s), 7.05 (1H, d, J = 7.6 Hz), 7.16-7.31 (1H, m), 7.34-7.59 (4H, m), 8.0 (2H, t, J = 1.2 Hz); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 16.1 (q, J_{C-P} = 6.0 Hz), 38.9 (d, J_{C-P} = 2.0 Hz), 42.3 (d, J_{C-P} = 128.0 Hz), 55.3, 62.8 (t, J_{C-P} = 8.0 Hz), 113.1, 116.6, 121.1, 125.4, 128.4, 128.9, 129.9, 133.1, 135.6, 137.4, 143.6, 159.9, 195.3 (d, J_{C-P} = 5.0 Hz), 196.3 (d, J_{C-P} = 15.0 Hz); $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$): δ 21.2; HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd. for $C_{23}H_{27}O_6PNa^+$ $[M+Na]^+$: 453.1437, found: 453.1436.

Diethyl (E)-(6-(2-methoxyphenyl)-1,4-dioxo-1-phenylhex-5-en-2-yl)phosphonate (**5d**): 80% yield (35 mg), pale yellow gummy

liquid, eluent: 60% EtOAc in hexane. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.09 (3H, t, J = 6.16 Hz), 1.17 (3H, t, J = 6.8 Hz), 3.19-3.34 (1H, m), 3.73-3.89 (1H, m), 3.82 (3H, s), 3.90-4.09 (4H, m), 4.58-4.75 (1H, m), 6.73 (1H, d, J = 16.0 Hz), 6.80-6.95 (2H, m), 7.25-7.35 (1H, m), 7.36-7.57 (4H, m), 7.89 (1H, d, J = 16.8 Hz), 8.01 (2H, t, J = 1.6 Hz); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 16.1 (q, $J_{C\text{-}P}$ = 7.0 Hz), 38.8, 42.3 (d, $J_{C\text{-}P}$ = 128.0 Hz), 55.4, 62.8 (q, $J_{C\text{-}P}$ = 7.0 Hz), 111.2, 120.7, 123.2, 125.6, 128.4, 128.7, 128.9, 131.9, 133.1, 137.5, 139.1, 158.6, 195.4 (d, $J_{C\text{-}P}$ = 5.0 Hz), 196.8 (d, $J_{C\text{-}P}$ = 16.0 Hz); ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$): δ 22.4; HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd. for $C_{23}H_{27}O_6PNa^+$ $[M+Na]^+$: 453.1437, found: 453.1434.

Diethyl (E)-(6-(4-fluorophenyl)-1,4-dioxo-1-phenylhex-5-en-2-yl)phosphonate (**5e**): 86% yield (36 mg), pale yellow gummy liquid, eluent: 60% EtOAc in hexane. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.09 (3H, t, J = 6.8 Hz), 1.16 (3H, t, J = 6.8 Hz), 3.15-3.31 (1H, m), 3.71-3.87 (1H, m), 3.89-4.11 (4H, m), 4.57-4.74 (1H, m), 6.64 (1H, d, J = 16.4 Hz), 7.28 (2H, d, J = 8.4 Hz), 7.34-7.56 (6H, m), 8.01 (2H, d, J = 7.6 Hz); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 16.1 (q, $J_{C\text{-}P}$ = 7.0 Hz), 38.9 (d, $J_{C\text{-}P}$ = 2.0 Hz), 42.3 (d, $J_{C\text{-}P}$ = 128.0 Hz), 62.8 (q, $J_{C\text{-}P}$ = 7.0 Hz), 116.1 (d, $J_{C\text{-}F}$ = 22.0 Hz), 124.8 (d, $J_{C\text{-}F}$ = 2.0 Hz), 128.4, 128.9, 130.3 (d, $J_{C\text{-}F}$ = 8.0 Hz), 130.5 (d, $J_{C\text{-}F}$ = 3.5 Hz), 133.2, 137.4, 142.3, 164.1 (d, $J_{C\text{-}F}$ = 250.0 Hz), 195.2 (d, $J_{C\text{-}P}$ = 5.0 Hz), 196.1 (d, $J_{C\text{-}P}$ = 16.0 Hz); ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$): δ 22.2; HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd. for $C_{22}H_{24}FO_5PNa^+$ $[M+Na]^+$: 441.1238, found: 441.1229.

Diethyl (E)-(6-(4-chlorophenyl)-1,4-dioxo-1-phenylhex-5-en-2-yl)phosphonate (**5f**): 84% yield (37 mg), pale yellow gummy liquid, eluent: 60% EtOAc in hexane. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.09 (3H, t, J = 7.2 Hz), 1.16 (3H, t, J = 6.8 Hz), 3.14-3.30 (1H, m), 3.71-3.87 (1H, m), 3.89-4.10 (4H, m), 4.56-4.76 (1H, m), 6.60 (1H, d, J = 16.4 Hz), 7.29 (2H, d, J = 8.4 Hz), 7.33-7.61 (6H, m), 8.01 (2H, d, J = 7.6 Hz); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 16.1 (d, $J_{C\text{-}P}$ = 6.0 Hz), 39.0 (d, $J_{C\text{-}P}$ = 2.0 Hz), 42.9 (d, $J_{C\text{-}P}$ = 118.0 Hz), 62.8 (t, $J_{C\text{-}P}$ = 8.0 Hz), 125.5, 128.4, 128.9, 129.2, 129.5, 132.7, 133.2, 136.6, 137.3, 142.1, 195.2 (d, $J_{C\text{-}P}$ = 5.0 Hz), 196.1 (d, $J_{C\text{-}P}$ = 15.0 Hz); ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$): δ 22.1; HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd. for $C_{22}H_{24}ClO_5PNa^+$ $[M+Na]^+$: 457.0943, found: 457.0945.

Diethyl (E)-(6-(4-bromophenyl)-1,4-dioxo-1-phenylhex-5-en-2-yl)phosphonate (**5g**): 82% yield (40 mg), pale yellow gummy liquid, eluent: 60% EtOAc in hexane. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.09 (3H, t, J = 7.2 Hz), 1.16 (3H, t, J = 7.2 Hz), 3.16-3.28 (1H, m), 3.71-3.86 (1H, m), 3.88-4.11 (4H, m), 4.56-4.74 (1H, m), 6.65 (1H, d, J = 16.0 Hz),), 7.32 (1H, d, J = 8.8 Hz), 7.37-7.55 (6H, m), 8.0 (2H, d, J = 7.2 Hz); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 16.1 (q, $J_{C\text{-}P}$ = 6.0 Hz), 39.0, 42.23 (d, $J_{C\text{-}P}$ = 128.0 Hz), 62.8 (t, $J_{C\text{-}P}$ = 8.0 Hz), 124.9, 125.5, 128.4, 128.9, 129.7, 132.2, 133.1, 133.2, 137.3, 142.2, 195.2 (d, $J_{C\text{-}P}$ = 5.0 Hz), 196.2 (d, $J_{C\text{-}P}$ = 16.0 Hz); ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$): δ 22.1; HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd. for $C_{22}H_{24}BrO_5PNa^+$ $[M+Na]^+$: 501.0437, found: 501.0439.

Diethyl (E)-(6-(2-nitrophenyl)-1,4-dioxo-1-phenylhex-5-en-2-yl)phosphonate (**5h**): 51% yield (23 mg), pale yellow gummy liquid, eluent: 60% EtOAc in hexane. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.09 (3H, t, J = 6.8 Hz), 1.18 (3H, t, J = 6.8 Hz), 3.18-3.35 (1H, m), 3.72-3.89 (1H, m), 3.90-4.11 (4H, m), 4.56-4.72 (1H, m), 6.54 (1H, d, J = 16.0 Hz), 7.33-7.66 (7H, m), 7.92-8.10 (4H, m); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 16.1 (q, $J_{C\text{-}P}$ = 7.0 Hz), 38.8, 42.3 (d, $J_{C\text{-}P}$ = 128.0 Hz), 62.9 (d, $J_{C\text{-}P}$ = 8.0 Hz), 125.1, 128.4, 128.9, 129.2, 129.8, 130.6, 130.7, 133.3, 133.7, 137.3, 139.1, 148.4, 195.2 (d, $J_{C\text{-}P}$ = 5.0 Hz), 196.0 (d, $J_{C\text{-}P}$ = 16.0 Hz); ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$): δ 21.8; HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd. for $C_{22}H_{24}NO_7PNa^+$ $[M+Na]^+$: 468.1183, found: 468.1179.

Diethyl (E)-(6-(3-nitrophenyl)-1,4-dioxo-1-phenylhex-5-en-2-yl)phosphonate (**5i**): 73% yield (33 mg), pale yellow gummy liquid, eluent: 60% EtOAc in hexane. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.09 (3H, t, J = 7.2 Hz), 1.17 (3H, t, J = 6.8 Hz), 3.18-3.33 (1H, m), 3.74-3.9 (1H, m) 3.91-4.09 (4H, m), 4.58-4.73 (1H, m), 6.79 (1H, d, J = 16.4 Hz), 7.36-7.63 (5H, m), 7.76 (1H, d, J = 7.6 Hz), 7.9 (2H, dd, J = 1.2 Hz), 8.16 (1H, dd, J = 1.2 Hz), 8.32 (1H, s); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 16.1 (q, $J_{C\text{-}P}$ = 6.0 Hz), 39.3 (d, $J_{C\text{-}P}$ = 2.0 Hz), 42.4 (d, $J_{C\text{-}P}$ = 128.0 Hz), 62.9 (q, $J_{C\text{-}P}$ = 7.0 Hz), 122.6, 124.8, 127.5, 128.4, 128.9, 130.0, 133.3, 133.9, 136.1, 137.3, 140.5, 148.7, 195.9 (d, $J_{C\text{-}P}$ = 5.0 Hz), 195.8 (d, $J_{C\text{-}P}$ = 15.0 Hz); ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$): δ 21.8; HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd. for $C_{22}H_{24}NO_7PNa^+$ $[M+Na]^+$: 468.1183, found: 468.1177.

Diethyl (E)-(6-(naphthalen-1-yl)-1,4-dioxo-1-phenylhex-5-en-2-yl)phosphonate (**5j**): 66% yield (30 mg) pale yellow gummy liquid, eluent: 60% EtOAc in hexane. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.1 (3H, t, J = 7.2 Hz), 1.19 (3H, t, J = 4.8 Hz), 3.24-3.39 (1H, m), 3.80-3.93 (1H, m), 3.94-4.11 (4H, m), 4.62-4.78 (1H, m), 6.78 (1H, d, J = 15.6 Hz), 7.34-7.58 (6H, m), 7.70 (1H, d, J = 7.2 Hz), 7.76-7.87 (2H, m), 7.99-8.14 (3H, m), 8.38 (2H, d, J = 16.0 Hz); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 16.1 (q, $J_{C\text{-}P}$ = 6.0 Hz), 39.5 (d, $J_{C\text{-}P}$ = 2.0 Hz), 42.4 (d, $J_{C\text{-}P}$ = 128.0 Hz), 62.8 (t, $J_{C\text{-}P}$ = 8.0 Hz), 123.2, 125.2, 125.4, 126.2, 126.9, 127.3, 128.5, 128.8, 128.9, 130.9, 131.5, 131.6, 133.2, 133.6, 137.4, 140.4, 195.3 (d, $J_{C\text{-}P}$ = 5.0 Hz), 196.2 (d, $J_{C\text{-}P}$ = 15.0 Hz); ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$): δ 22.2; HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd for $C_{26}H_{27}O_5PNa^+$ $[M+Na]^+$: 473.1489, found: 473.1483.

Diethyl (E)-(1,4-dioxo-1-phenyl-6-(thiophen-2-yl)hex-5-en-2-yl)phosphonate (**5k**): 76% yield (31 mg), pale yellow gummy liquid, eluent: 60% EtOAc in hexane. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.09 (3H, t, J = 7.2 Hz), 1.16 (3H, t, J = 7.2 Hz), 3.11-3.27 (1H, m), 3.66-3.83 (1H, m), 3.88-4.11 (4H, m), 4.56-4.74 (1H, m), 6.48 (1H, d, J = 15.6 Hz), 6.95-7.04 (1H, m), 7.22 (1H, d, J = 4.8 Hz), 7.31-7.56 (4H, m), 7.64 (1H d, J = 16.0 Hz), 7.99 (2H, t, J = 1.2 Hz); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 16.1 (q, $J_{C\text{-}P}$ = 6.0 Hz), 39.0 (d, $J_{C\text{-}P}$ = 2.0 Hz), 42.3 (d, $J_{C\text{-}P}$ = 128.0 Hz), 62.8 (t, $J_{C\text{-}P}$ = 7.0 Hz), 123.7, 128.3, 128.4, 128.9, 129.2, 131.9, 133.1, 136.0, 137.4, 139.6, 195.3 (d, $J_{C\text{-}P}$ = 5.0 Hz), 195.7 (d, $J_{C\text{-}P}$ = 16.0 Hz); ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$): δ 22.2; HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd. for $C_{20}H_{23}O_5PSNa^+$ $[M+Na]^+$: 429.0897, found: 429.0893.

Diethyl (E)-(1,4-dioxo-1-phenylhept-5-en-2-yl)phosphonate (**5l**): 67% yield (23 mg), pale yellow gummy liquid, eluent: 60% EtOAc in hexane. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.07 (3H, t, J = 6.4 Hz), 1.15 (3H, t, J = 6.8 Hz), 1.84 (3H, d, J = 6.8 Hz), 3.01-3.18 (1H, m), 3.56-3.75 (1H, m), 3.85-4.13 (4H, m), 4.49-4.70 (1H, m), 6.06 (1H, d, J = 16.0 Hz), 6.77-6.99 (1H, m), 7.39 (3H, t, J = 7.6 Hz), 7.48 (2H, t, J = 7.2 Hz), 7.98 (2H, d, J = 7.6 Hz); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 16.1 (q, $J_{C\text{-}P}$ = 6.0 Hz), 38.1 (d, $J_{C\text{-}P}$ = 2.0 Hz), 42.2 (d, $J_{C\text{-}P}$ = 128.0 Hz), 62.8 (t, $J_{C\text{-}P}$ = 7.0 Hz), 128.4, 128.9, 130.9, 133.1, 137.4, 144.1, 195.4 (d, $J_{C\text{-}P}$ = 5.0 Hz), 196.3 (d, $J_{C\text{-}P}$ = 16.0 Hz); ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$): δ 22.3; HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd. for $C_{17}H_{23}O_5PNa^+$ $[M+Na]^+$: 361.1176, found: 361.1172.

Diethyl (E)-(1-(4-methoxyphenyl)-1,4-dioxo-6-phenylhex-5-en-2-yl)phosphonate (**5m**): 88% yield (38 mg), pale yellow gummy liquid, eluent: 60% EtOAc in hexane. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.21 (3H, t, J = 6.8 Hz), 1.25 (3H, t, J = 7.2 Hz), 3.21-3.36 (1H, m), 3.80-3.94 (4H, m), 3.99-4.18 (4H, m), 4.62-4.78 (1H, m), 6.74 (1H, d, J = 16.4 Hz), 6.97 (2H, d, J = 8.8 Hz), 7.39 (3H, t, J = 3.6 Hz), 7.53 (2H, t, J = 3.6 Hz), 7.61 (1H, d, J = 16.0 Hz), 8.09 (2H, d, J = 8.4 Hz); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 16.2 (t, $J_{C\text{-}P}$ = 7.0 Hz), 38.8, 41.8 (d, $J_{C\text{-}P}$ = 128.0 Hz), 55.5, 62.8 (t, $J_{C\text{-}P}$ = 6.0 Hz), 113.6, 125.1, 128.3, 128.9, 130.1, 130.6, 131.4, 134.2, 143.6, 163.6, 193.3 (d, $J_{C\text{-}P}$ = 4.0 Hz), 196.5 (d, $J_{C\text{-}P}$ = 15.0 Hz); ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$): δ 22.7; HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd. for $C_{23}H_{27}O_6PNa^+$ $[M+Na]^+$: 453.1438, found: 453.1435.

Diethyl (E)-(1-(3-chlorophenyl)-1,4-dioxo-6-phenylhex-5-en-2-yl)phosphonate (**5n**): 85% yield (37 mg), pale yellow gummy liquid, eluent: 60% EtOAc in hexane. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.2 (3H, t, J = 6.8 Hz), 1.27 (3H, t, J = 7.2 Hz), 3.26-3.42 (1H, m), 3.79-3.93 (1H, m), 3.99-4.17 (4H, m), 4.55-4.68 (1H, m), 6.74 (1H, d, J = 16.0 Hz), 7.37-7.43 (3H, m), 7.45 (1H, d, J = 7.6 Hz), 7.50-7.58 (3H, m), 7.62 (1H, d, J = 16.4 Hz), 7.98 (1H, d, J = 8.0 Hz), 8.04 (1H, s); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 16.2 (q, $J_{C\text{-}P}$ = 7.0 Hz), 39.1, 42.6 (d, $J_{C\text{-}P}$ = 129.0 Hz), 62.9 (t, $J_{C\text{-}P}$ = 4.0 Hz), 124.9, 127.0, 128.4, 128.9, 129.0, 129.7, 130.8, 133.0, 134.1, 134.7, 138.9, 143.9, 194.2 (d, $J_{C\text{-}P}$ = 5.0 Hz), 196.2 (d, $J_{C\text{-}P}$ = 16.0 Hz); ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$): δ 21.6; HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd. for $C_{22}H_{24}ClO_5PNa^+$ $[M+Na]^+$: 457.0943, found: 457.0944.

Diethyl (E)-(1,4-dioxo-6-phenyl-1-(thiophen-2-yl)hex-5-en-2-yl)phosphonate (**5o**): 79% yield (32 mg), pale yellow gummy liquid, eluent: 60% EtOAc in hexane. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.17-1.36 (6H, m), 3.21-3.37 (1H, m), 3.73-3.91 (1H, m), 4.01-4.24 (4H, m), 4.45-4.63 (1H, m), 6.74 (1H, d, J = 16.0 Hz), 7.17 (1H, t, J = 4.4 Hz), 7.40 (3H, t, J = 3.6 Hz), 7.53 (2H, t, J = 3.6 Hz), 7.62 (1H, d, J = 16.0 Hz), 7.68 (1H, d, J = 4.8 Hz), 7.97 (1H, d, J = 3.6 Hz); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 16.2 (t, $J_{C\text{-}P}$ = 5.0 Hz), 38.4, 43.7 (d, $J_{C\text{-}P}$ = 129.0 Hz), 62.9 (t, $J_{C\text{-}P}$ = 7.0 Hz), 125.0, 128.1, 128.3, 128.9, 130.7, 133.7, 134.1, 134.4, 143.7, 144.0, 187.2 (d, $J_{C\text{-}P}$ = 5.0 Hz), 196.2 (d, $J_{C\text{-}P}$ = 16.0 Hz); ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$): δ 21.9; HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd. for $C_{20}H_{23}O_5PNa^+$ $[M+Na]^+$: 429.0897, found: 429.0901.

Diethyl (2,5-diphenyl-1H-pyrrol-3-yl)phosphonate (**6a**): 91% yield (32 mg), pale yellow gummy liquid, eluent: 60% EtOAc in hexane. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.14 (6H, t, J = 7.2 Hz), 3.85-4.01 (4H, m), 6.86 (1H, q, J = 2.8 Hz), 7.20-7.43 (6H, m), 7.61 (2H, d, J = 8.0 Hz), 7.72 (2H, d, J = 7.2 Hz), 9.78 (1H, s); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 16.04 (d, $J_{C\text{-}P}$ = 6.7 Hz), 61.6 (d, $J_{C\text{-}P}$ = 5.2 Hz), 106.8 (d, $J_{C\text{-}P}$ = 214.2 Hz), 112.4 (d, $J_{C\text{-}P}$ = 12.5 Hz), 124.3, 126.8, 128.0, 128.2, 128.3, 128.8, 131.5 (d, $J_{C\text{-}P}$ = 0.9 Hz), 131.8, 132.9 (d, $J_{C\text{-}P}$ = 15.5 Hz), 138.6 (d, $J_{C\text{-}P}$ = 22.7 Hz); ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$): δ 17.7; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd. for $C_{20}H_{22}NO_3PH^+$: 356.1411, found: 356.1414.

Diethyl (2-phenyl-5-(p-tolyl)-1H-pyrrol-3-yl)phosphonate (**6b**): 93% yield (34 mg), pale yellow gummy liquid, eluent: 60% EtOAc in hexane. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.01 (6H, t, J = 6.8 Hz), 2.25 (3H, s) 3.70-3.92 (4H, m), 6.71 (1H, q, J = 2.8 Hz), 7.07 (2H, d, J = 8.0 Hz), 7.13-7.32 (3H, m), 7.43 (2H, d, J = 8.0 Hz), 7.61 (2H, d, J = 7.2 Hz), 9.93 (1H, s); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 16.0 (d, $J_{C\text{-}P}$ = 7.0 Hz), 21.1, 61.5 (d, $J_{C\text{-}P}$ = 5.2 Hz), 106.4 (d, $J_{C\text{-}P}$ = 214.0 Hz), 111.9 (d, $J_{C\text{-}P}$ = 12.6 Hz), 124.3, 127.8, 128.1, 128.4, 128.8, 129.4, 131.8, 133.2 (d, $J_{C\text{-}P}$ = 16.0 Hz), 136.4, 138.3 (d, $J_{C\text{-}P}$ = 22.0 Hz); ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$): δ 17.9; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd. for $C_{21}H_{24}NO_3PH^+$ 370.1567, found: 370.1566.

Diethyl (5-(4-bromophenyl)-2-phenyl-1H-pyrrol-3-yl)phosphonate (**6c**): 95% yield (41 mg), pale yellow gummy liquid, eluent: 60% EtOAc in hexane. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.11 (6H, t, J = 7.2 Hz), 3.78-4.01 (4H, m), 6.78 (1H, q, J = 4.0 Hz), 7.15-7.31 (3H, m), 7.46 (4H, q, J = 4.8 Hz), 7.67 (2H, d, J = 7.6 Hz), 10.27 (1H, s); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 16.0 (d, $J_{C\text{-}P}$ = 7 Hz), 61.7 (d, $J_{C\text{-}P}$ = 6.0 Hz), 107.0 (d, $J_{C\text{-}P}$ = 214.0 Hz), 112.8 (d, $J_{C\text{-}P}$ = 12.5 Hz), 120.4, 125.9, 128.1, 128.2, 128.4, 130.6, 131.6, 131.8, 131.9 (d, $J_{C\text{-}P}$ = 15.0 Hz), 139.1 (d, $J_{C\text{-}P}$ = 23.0 Hz); ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$): δ 17.4; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd. for $C_{20}H_{21}BrNO_3PH^+$ 434.0516, found: 434.0518.

Diethyl (E)-(2-phenyl-5-styryl-1H-pyrrol-3-yl)phosphonate (**6d**): 78% yield (30 mg), pale yellow gummy liquid, eluent: 60% EtOAc in hexane. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.10 (6H, t, J = 7.2 Hz), 3.84-4.01 (4H, m), 6.66 (1H, s), 6.91 (2H, s), 7.18 (1H, t, J = 7.2), 7.24-7.34 (5H, m), 7.39 (2H, d, J = 8.0 Hz), 7.68 (2H, d, J = 7.6 Hz), 10.09 (1H, s); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 16.0 (d, $J_{C\text{-}P}$ = 7.0 Hz), 61.7 (d, $J_{C\text{-}P}$ = 5.0 Hz), 106.3 (d, $J_{C\text{-}P}$ = 215.0 Hz), 115.1 (d, $J_{C\text{-}P}$ = 12.0 Hz), 117.9, 125.5, 125.9, 127.1, 127.9, 128.1, 128.2, 128.6, 131.6, 131.8 (d, $J_{C\text{-}P}$ = 16.0 Hz), 137.3, 138.7 (d, $J_{C\text{-}P}$ = 23.0 Hz); ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$): δ 17.7; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd. for $C_{22}H_{24}NO_3PH^+$: 382.1567, found: 382.1567.

Diethyl (2-(naphthalen-1-yl)-5-phenyl-1H-pyrrol-3-yl)phosphonate (**6e**): 89% yield (36 mg), brown gummy liquid, eluent: 60% EtOAc in hexane. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.11 (6H, t, J = 6.8 Hz), 3.82-4.05 (4H, m), 6.79 (1H, s), 7.21-7.41 (3H, m), 7.41-7.60 (4H, m), 7.68-7.90 (4H, m), 8.21-8.33 (1H, m), 9.55 (1H, s); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 16.0 (d, $J_{C\text{-}P}$ = 7.0 Hz), 61.6 (d, $J_{C\text{-}P}$ = 10.0 Hz), 106.4 (d, $J_{C\text{-}P}$ = 215.0 Hz), 115.8 (d, $J_{C\text{-}P}$ = 12.0 Hz), 122.2, 125.4, 126.0, 126.5, 128.0 (d, $J_{C\text{-}P}$ = 8.0 Hz), 128.1, 128.2, 128.3, 129.9, 131.2, 131.2 (d, $J_{C\text{-}P}$ = 16.0 Hz), 131.7, 133.8, 138.2 (d, $J_{C\text{-}P}$ = 23.0 Hz); ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$): δ 17.8; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd. for $C_{24}H_{24}NO_3PH^+$: 406.1567, found: 406.1563.

Diethyl (5-phenyl-2-(thiophen-2-yl)-1H-pyrrol-3-yl)phosphonate (**6f**): 86% yield (31 mg), brown gummy liquid, eluent: 60% EtOAc in hexane. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.13 (6H, t, J = 6.8 Hz), 3.84-4.08 (4H, m), 6.75 (1H, s), 7.01 (1H, t, J = 4.0 Hz), 7.19 (2H, d, J = 4.4), 7.28-7.42 (3H, m), 7.68 (2H, d, J = 7.6 Hz), 9.37 (1H, s); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 16.0 (d, $J_{C\text{-}P}$ = 7.0 Hz), 61.7 (d, $J_{C\text{-}P}$ = 5.0 Hz), 106.6 (d, $J_{C\text{-}P}$ = 214.0 Hz), 112.9 (d, $J_{C\text{-}P}$ = 13.0 Hz), 122.2, 123.4, 127.6, 127.6 (d, $J_{C\text{-}P}$ = 16.0 Hz), 128.0, 128.2, 128.3, 131.4, 134.6, 138.3 (d, $J_{C\text{-}P}$ = 23.0 Hz); ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$): δ 17.3; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd. for $C_{18}H_{20}NO_3PSH^+$: 362.0975, found: 362.0970.

Diethyl (2,5-diphenylfuran-3-yl)phosphonate (**7a**): 79% yield (28 mg), pale yellow gummy liquid, eluent: 60% EtOAc in hexane. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.19 (6H, t, J = 7.2 Hz), 3.92-4.18 (4H, m), 6.93 (1H, d, J = 3.6 Hz), 7.24 (1H, d, J = 7.6 Hz), 7.29-7.43 (5H, m), 7.67 (2H, d, J = 7.6 Hz), 7.98 (2H, d, J = 7.6 Hz); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 16.2 (d, $J_{C\text{-}P}$ = 6.7 Hz), 62.3 (d, $J_{C\text{-}P}$ = 5.3 Hz), 109.5 (d, $J_{C\text{-}P}$ = 210.1 Hz), 110.8, 110.9, 124.0, 127.4, 128.1, 128.4, 128.8, 129.2, 129.6, 152.9 (d, $J_{C\text{-}P}$ = 15.2 Hz), 157.3 (d, $J_{C\text{-}P}$ = 24.3 Hz); ^{31}P{^{1}H}

NMR (162 MHz, $CDCl_3$): δ 14.0; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd. for $C_{20}H_{21}O_4PH^+$ 357.1251, found: 357.1257.

Diethyl (2-phenyl-5-(p-tolyl)-furan-3-yl)phosphonate (**7b**): 85% yield (32 mg), pale yellow gummy liquid, eluent: 60% EtOAc in hexane. ^1H NMR (400 MHz, $CDCl_3$): δ 1.17 (6H, t, J = 7.2 Hz), 2.29 (3H, s), 3.91-4.20 (4H, m), 6.87 (1H, d, J = 4.0 Hz), 7.14 (2H, d, J = 7.6 Hz), 7.29 (1H, t, J = 7.2 Hz), 7.36 (2H, t, J = 8.0 Hz), 7.54 (2H, d, J = 8.0 Hz), 7.96 (2H, d, J = 7.6 Hz); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 16.1 (d, $J_{C\text{-}P}$ = 6.0 Hz), 21.3, 62.2 (d, $J_{C\text{-}P}$ = 5.0 Hz), 109.2 (d, $J_{C\text{-}P}$ = 211.0 Hz), 110.0 (d, $J_{C\text{-}P}$ = 11.3 Hz), 123.9, 126.8, 127.3, 128.3, 129.0, 129.4, 129.6, 138.1, 153.2 (d, $J_{C\text{-}P}$ = 15.0 Hz), 156.9 (d, $J_{C\text{-}P}$ = 24.0 Hz); $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$): δ 14.3; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd. for $C_{21}H_{23}O_4PH^+$ 371.1407, found: 371.1406.

Diethyl (5-(4-bromophenyl)-2-phenylfuran-3-yl)phosphonate (**7c**): 83% yield (36 mg), pale yellow gummy liquid, eluent: 60% EtOAc in hexane. ^1H NMR (400 MHz, $CDCl_3$): δ 1.25 (6H, t, J = 7.2 Hz), 3.98-4.25 (4H, m), 7.0 (1H, d, J = 4.0 Hz), 7.34-7.63 (7H, m), 8.02 (2H, d, J = 8.0 Hz); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 16.1 (d, $J_{C\text{-}P}$ = 7.0 Hz), 62.3 (d, $J_{C\text{-}P}$ = 6.0 Hz), 109.7 (d, $J_{C\text{-}P}$ = 211.0 Hz), 111.3 (d, $J_{C\text{-}P}$ = 11.0 Hz), 121.9, 125.4, 127.4, 128.3, 128.5, 129.2, 129.3, 131.9, 151.8 (d, $J_{C\text{-}P}$ = 16.0 Hz), 157.5 (d, $J_{C\text{-}P}$ = 24.0 Hz); $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$): δ 13.6; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd. for $C_{20}H_{20}BrO_4PH^+$ 435.0356, found: 435.0359.

Diethyl (E)-(2-phenyl-5-styrylfuran-3-yl)phosphonate (**7d**): 71% yield (27 mg), pale yellow gummy liquid, eluent: 60% EtOAc in hexane. ^1H NMR (400 MHz, $CDCl_3$): δ 1.25 (6H, t, J = 6.8 Hz), 3.99-4.21 (4H, m), 6.70 (1H, d, J = 4.0 Hz), 6.89 (1H, d, J = 16.4 Hz), 7.15 (1H, d, J = 16.4 Hz), 7.28 (1H, d, J = 7.2 Hz), 7.33-7.42 (3H, m), 7.43-7.52 (4H, m), 8.04 (2H, d, J = 7.6 Hz); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 16.1 (d, $J_{C\text{-}P}$ = 6.0 Hz), 62.3 (d, $J_{C\text{-}P}$ = 6.0 Hz), 109.4 (d, $J_{C\text{-}P}$ = 211.0 Hz), 114.1 (d, $J_{C\text{-}P}$ = 11.0 Hz), 115.2, 126.4, 127.4, 128.0, 128.3, 128.7, 128.8, 129.2, 129.4, 136.5, 152.2 (d, $J_{C\text{-}P}$ = 15.0 Hz), 157.3 (d, $J_{C\text{-}P}$ = 24.0 Hz); $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$): δ 13.9; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd. for $C_{22}H_{23}O_4PH^+$ 383.1407, found: 383.1406.

Diethyl (2-(naphthalen-1-yl)-5-phenylfuran-3-yl)phosphonate (**7e**): 88% yield (36 mg), pale yellow gummy liquid, eluent: 60% EtOAc in hexane. ^1H NMR (400 MHz, $CDCl_3$): δ 1.29 (6H, t, J = 6.8 Hz), 4.06-4.28 (4H, m), 7.09 (1H, d, J = 3.6 Hz), 7.34-7.64 (6H, m), 7.81 (1H, d, J = 7.2 Hz), 7.87 (2H, t, J = 9.2 Hz), 8.10 (2H, d, J = 8.0 Hz), 8.44 (1H, d, J = 8.0 Hz); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 16.2 (d, $J_{C\text{-}P}$ = 7.0 Hz), 62.3 (d, $J_{C\text{-}P}$ = 6.0 Hz), 109.3 (d, $J_{C\text{-}P}$ = 211.0 Hz), 114.8 (d, $J_{C\text{-}P}$ = 11.0 Hz), 125.1, 125.2, 126.0, 126.4, 126.9, 127.1, 127.4, 128.4, 128.6, 129.2 (d, $J_{C\text{-}P}$ = 5.0 Hz), 129.6, 130.1, 133.9, 152.5 (d, $J_{C\text{-}P}$ = 16.0 Hz), 157.7 (d, $J_{C\text{-}P}$ = 24.0 Hz); $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$): δ 14.1; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd. for $C_{24}H_{23}O_4PH^+$: 407.1407, found: 407.1405.

Diethyl (5-phenyl-2-(thiophen-2-yl)furan-3-yl)phosphonate (**7f**): 79% yield (29 mg), pale yellow gummy liquid, eluent: 60% EtOAc in hexane. ^1H NMR (400 MHz, $CDCl_3$): δ 1.26 (6H, t, J = 7.2 Hz), 4.01-4.22 (4H, m), 6.85 (1H, d, J = 4.0 Hz), 7.07 (1H, t, J = 4.4 Hz), 7.29 (1H, d, J = 5.2 Hz), 7.35 (1H, d, J = 4.0 Hz) 7.36-7.52 (3H, m), 8.02 (2H, d, J = 7.6 Hz); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 16.1 (d, $J_{C\text{-}P}$ = 7.0 Hz), 62.3 (d, $J_{C\text{-}P}$ = 5.0 Hz), 109.4 (d, $J_{C\text{-}P}$ = 212.0 Hz), 110.6 (d, $J_{C\text{-}P}$ = 11.0 Hz), 123.6, 125.1, 127.3, 127.7, 128.3, 129.2, 129.3, 132.2, 148.6 (d, $J_{C\text{-}P}$ = 16.0 Hz), 156.8 (d, $J_{C\text{-}P}$ = 24.0 Hz); $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$): δ 13.6; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd. for $C_{18}H_{19}O_4PH^+$: 363.0815, found: 363.0810.

Diethyl (2,5-diphenylthiophen-3-yl)phosphonate (**8a**): 81% yield (30 mg), pale yellow gummy liquid, eluent: 60% EtOAc in hexane. ^1H NMR (400 MHz, $CDCl_3$): δ 1.07 (6H, t, J = 6.8 Hz), 3.82-4.05 (4H, m), 7.20 (1H, d, J = 14.4 Hz), 7.28-7.38 (5H, m), 7.53 (3H, t, J = 6.8 Hz), 7.61 (2H, t, J = 2.4 Hz); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 16.0 (d, $J_{C\text{-}P}$ = 6.8 Hz), 62.1 (d, $J_{C\text{-}P}$ = 5.6 Hz), 125.7 (d, $J_{C\text{-}P}$ = 192.5 Hz), 125.8, 128.0, 128.1, 128.2 (d, $J_{C\text{-}P}$ = 16.0 Hz), 128.8, 129.0, 129.6, 133.1, 133.2 (d, $J_{C\text{-}P}$ = 2.0 Hz), 143.7 (d, $J_{C\text{-}P}$ = 19.0 Hz), 151.5 (d, $J_{C\text{-}P}$ = 16.0 Hz); $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$): δ 12.8; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd. for $C_{20}H_{21}O_3PSH^+$ 373.1022, found: 373.1023.

Diethyl (2-phenyl-5-(p-tolyl)-thiophen-3-yl)phosphonate (**8b**): 88% yield (34 mg), pale yellow gummy liquid, eluent: 60% EtOAc in hexane. ^1H NMR (400 MHz, $CDCl_3$): δ 1.15 (6H, t, J = 6.8 Hz), 2.38 (3H, s), 3.90-4.11 (4H, m), 7.21 (2H, d, J = 8.0 Hz), 7.41 (3H, d, J = 6.8 Hz), 7.50 (2H, d, J = 8.0 Hz), 7.57 (1H, d, J = 4.4 Hz), 7.67 (2H, t, J = 5.6 Hz); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 16.1 (d, $J_{C\text{-}P}$ = 7.0 Hz), 21.21, 62.1 (d, $J_{C\text{-}P}$ = 6.0 Hz), 125.7 (d, $J_{C\text{-}P}$ = 192.0 Hz), 125.8, 127.7 (d, $J_{C\text{-}P}$ = 16.0 Hz), 128.1, 128.7, 129.6, 129.7, 130.5, 133.3 (d, $J_{C\text{-}P}$ = 2.0 Hz), 138.1, 143.9 (d, $J_{C\text{-}P}$ = 19.0 Hz), 151.0 (d, $J_{C\text{-}P}$ = 16.0 Hz); $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$): δ 12.9; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd. for $C_{21}H_{23}O_3PSH^+$ 387.1178, found: 387.1178.

Diethyl (5-(4-bromophenyl)-2-phenylthiophen-3-yl) phosphonate (**8c**): 86% yield (39 mg), pale yellow gummy liquid eluent: 60% EtOAc in hexane. ^1H NMR (400 MHz, $CDCl_3$): δ 1.14 (6H, t, J = 7.2 Hz), 3.88-4.15 (4H, m), 7.36-7.55 (7H, m), 7.61 (1H, d, J = 4.8 Hz), 7.66 (2H, t, J = 3.6 Hz); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 16.0 (d, $J_{C\text{-}P}$ = 7.0 Hz), 62.1 (d, $J_{C\text{-}P}$ = 8.0 Hz), 121.9, 126.2 (d, $J_{C\text{-}P}$ = 193.0 Hz), 127.3, 128.2, 128.6 (d, $J_{C\text{-}P}$ = 17.0 Hz), 128.9, 129.6, 132.1, 132.2, 133.0 (d, $J_{C\text{-}P}$ = 3.0 Hz), 142.3 (d, $J_{C\text{-}P}$ = 19.0 Hz), 151.8 (d, $J_{C\text{-}P}$ = 16.0 Hz); $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$): δ 12.4; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd. for $C_{20}H_{20}BrO_3PSH^+$ 451.0127, found: 451.0129.

Diethyl (2,3,6-triphenyl-2,5-dihydropyridazin-4-yl)phosphonate (**9a**): 93% yield (41 mg), yellow solid (mp 158-160 °C), eluent: 60% EtOAc in hexane. ^1H NMR (400 MHz, $CDCl_3$): δ 0.98 (6H, t, J = 7.2 Hz), 3.45 (2H, d, J = 9.2 Hz), 3.59-3.70 (2H, m), 3.71-3.82 (2H, m), 6.85 (1H, t, J = 7.2 Hz), 7.03 (2H, t, J = 8.0 Hz), 7.07-7.25 (7H, m), 7.31-7.42 (3H, m), 7.90 (2H, d, J = 6.4 Hz); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 16.0 (d, $J_{C\text{-}P}$ = 6.8 Hz), δ 26.0 (d, $J_{C\text{-}P}$ = 8.7 Hz), 61.3 (d, $J_{C\text{-}P}$ = 5.7 Hz), 90.3 (d, $J_{C\text{-}P}$ = 206.5 Hz), 123.5, 124.2, 126.9, 127.4, 128.1, 128.5, 128.7, 129.6, 130.9, 133.5 (d, $J_{C\text{-}P}$ = 3.1 Hz), 135.1, 143.7 (d, $J_{C\text{-}P}$ = 2.5 Hz), 144.0 (d, $J_{C\text{-}P}$ = 4.3 Hz), 150.2 (d, $J_{C\text{-}P}$ = 21.9 Hz); $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$): δ 19.17; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd. for $C_{26}H_{27}N_2O_3PH^+$ 447.1833, found: 447.1838.

Diethyl (2,3-diphenyl-6-(p-tolyl)-2,5-dihydropyridazin-4-yl)phosphonate (**9b**): 98% yield (45 mg), yellow solid (mp 160-162 °C), eluent: 60% EtOAc in hexane. ^1H NMR (400 MHz, $CDCl_3$): δ 1.08 (6H, t, J = 7.2 Hz), 2.43 (3H, s), 3.52 (2H, d, J = 9.2 Hz), 3.68-3.79 (2H, m), 3.80-3.91 (2H, m), 6.94 (1H, t, J = 7.2 Hz), 7.12 (2H, t, J = 8.0 Hz), 7.16-7.34 (9H, m), 7.89 (2H, d, J = 8.0 Hz); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 16.0 (d, $J_{C\text{-}P}$ = 7.0 Hz), 21.4, 26.0 (d, $J_{C\text{-}P}$ = 8.0 Hz), 61.3 (d, $J_{C\text{-}P}$ = 6.0 Hz), 90.2 (d, $J_{C\text{-}P}$ = 206.0 Hz), 123.5, 124.1, 126.8, 127.4, 128.1,

128.7, 129.3, 131.0, 132.3, 133.6 (d, J_{C-P} = 3.0 Hz), 139.8, 143.8 (d, J_{C-P} = 2.0 Hz), 144.1 (d, J_{C-P} = 5.0 Hz), 150.3 (d, J_{C-P} = 22.0 Hz); $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$): δ 19.3; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd. for $C_{27}H_{29}N_2O_3PH^+$ 461.1989, found: 461.1986.

Diethyl (6-(4-bromophenyl)-2,3-diphenyl-2,5-dihydrpyridazin-4-yl)phosphonate (**9c**): 95% yield (50 mg), yellow solid (mp 179-182 °C), eluent: 60% EtOAc in hexane. ^1H NMR (400 MHz, $CDCl_3$): δ 1.08 (6H, t, J = 7.2 Hz), 3.51 (2H, d, J = 8.8 Hz), 3.67-3.79 (2H, m), 3.80-3.92 (2H, m), 6.96 (1H, t, J = 7.2 Hz), 7.13 (2H, t, J = 8.0 Hz), 7.17-7.33 (7H, m), 7.59 (2H, d, J = 8.4 Hz), 7.86 (2H, d, J = 8.0 Hz); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 16.0 (d, J_{C-P} = 7.0 Hz), δ 25.7 (d, J_{C-P} = 9.0 Hz), 61.3 (d, J_{C-P} = 6.0 Hz), 90.3 (d, J_{C-P} = 206.0 Hz), 123.5, 123.9, 124.4, 127.4, 128.1, 128.3, 128.8, 130.9, 131.7, 133.3 (d, J_{C-P} = 3.0 Hz), 134.0, 142.7 (d, J_{C-P} = 4.0 Hz), 143.5 (d, J_{C-P} = 2.0 Hz), 150.1 (d, J_{C-P} = 22.0 Hz); $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$): δ 19.02; HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd. for $C_{26}H_{26}BrN_2O_3PNa^+$ 547.0757, found: 547.0756

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website.

^1H, $^{13}C\{^1H\}$ and $^{31}P\{^1H\}$ NMR Spectra

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Ram Subhawan Verma and Monika Mishra have made equal contribution to this manuscript.

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REFERENCES

1. For selected reviews and examples, see: (a) Paul, S.; Roy, S.; Monfregola, L.; Shang, S.; Shoemaker, R.; Caruthers M. H. Oxidative substitution of boranephosphonate diesters as a route to post-synthetically modified DNA. *J. Am. Chem. Soc.* **2015**, *137*, 3253−3264. (b) Fu, W. C.; So, C. M.; Chow, W. K.; Yuen, O. Y.; Kwong, F. Y. Design of an indolylphosphine ligand for reductive elimination-demanding monoarylation of acetone using aryl chlorides. *Org. Lett.* **2015**, *17*, 4612–4615. (c) Zheng, B.; Jia, T.; Walsh, P. J. Palladium-catalyzed direct α-arylation of methyl sulfones with aryl bromides. *Org. Lett.* **2013**, *15*, 1690–1693. (d) Jeon, S. O.; Lee, J. Y. Comparison of symmetric and asymmetric bipolar type high triplet energy host materials for deep blue phosphorescent organic light-emitting diodes. *J. Mater. Chem.* **2012**, *22*, 7239–7244. (e) Alexandre, F. R.; Amador, A.; Bot, S.; Caillet, C.; Convard, T.; Jakubik, J.; Musiu, C.; Poddesu, B.; Vargiu, L.; Liuzzi, M.; Roland, A.; Seifer, M.; Standring, D.; Storer, R.; Dousson C. B. Synthesis and biological evaluation of aryl-phospho-indole as novel HIV-1 non-nucleoside reverse transcriptase inhibitors. *J. Med. Chem.* **2011**, *54*, 392–395. (f) Fernández-Pérez, H.; Etayo, P.; Panossian, A.; Vidal-Ferran, A. Phosphine−phosphinite and phosphine−phosphite ligands: Preparation and applications in asymmetric catalysis. *Chem. Rev.* **2011**, *111*, 2119–2176.

2. For selected examples, see: (a) Guo, C.; Sun, S.; He, Q.; Lynch, V. M.; Sessler, J. L. Pyrene-linked formylated bis(dipyrromethane): A fluorescent probe for dihydrogen phosphate. *Org. Lett.* **2018**, *20*, 5414–5417. (b) Jiang, H.; Paixão, M. W.; Monge, D.; Jørgensen, K. A. Acyl phosphonates: Good hydrogen bond acceptors and ester/amide equivalents in asymmetric organocatalysis. *J. Am. Chem. Soc.* **2010**, *132*, 2775–2783.

3. (a) Mishra, A.; Deb, I. Palladium-catalyzed oxidative cyclization for the synthesis of indolyl/pyrrolyl 3-phosphonates. *Adv. Synth. Catal.* **2016**, *358*, 2267–2272. (b) Debrouwer, W.; Heugebaert, T. S. A.; Stevens, C. V. Preparation of tetrasubstituted 3-phosphonopyrroles through hydroamination: scope and limitations. *J. Org. Chem.* **2014**, *79*, 4322–4331. (c) Lonzi, G.; Lõpez, L. A. Regioselective synthesis of functionalized pyrroles via gold (I)-catalyzed [3+ 2] cycloaddition of stabilized vinyl diazo derivatives and nitriles. *Adv. Synth. Catal.* **2013**, *355*, 1948–1954.

4. Yu, Y.; Yi, S.; Zhu, C.; Hu, W.; Gao, B.; Chen, Y.; Wu, W.; Jiang, H. Csp3–P versus Csp2–P bond formation: Catalyst-controlled highly regioselective tandem teaction of ene-yne-ketones with H-phosphonates. *Org. Lett.* **2016**, *18*, 400–403.

5. (a) Isshiki, R.; Muto, K.; Yamaguchi, J. Decarbonylative C–P bond formation using aromatic esters and organophosphorus compound. *Org. Lett.* **2018**, *20*, 1150–1153. (b) Min, M.; Kang, D.; Jung, S.; Hong, S. Rhodium-catalyzed direct C–H phosphorylation of (hetero)arenes suitable for late-stage functionalization. *Adv. Synth. Catal.* **2016**, *358*, 1296–1301. (c) Lilley, M.; Mambwe, B.; Jackson, R. F. W.; Muimo, R. 4-Phosphothiophen-2-yl alanine: A new 5-membered analogue of phosphotyrosine. *Chem. Commun.* **2014**, *50*, 9343–9345.

6. (a) Bhaumik, A.; Azaz, T.; Singh, V.; Khatana, A. K.; Tiwari B. Carbene/base-mediated redox alkenylation of isatins using β-substituted organoselenones and aldehydes. *J. Org. Chem.* **2019**, *84*, 14898-14903. (b) Verma, R. S.; Pandey, C. B.; Kumar, S.; Tiwari, B. Carbene-catalyzed tandem [1,2]-phospha-Brook/[1,4]-phosphonate rearrangement: Access to α-ketophosphates via controlled cross-acyloin condensation. *J. Org. Chem.* **2018**, *83*, 9478−9483. (c) Bhaumik, A.; Verma, R. S.; Tiwari, B. Direct construction of 2,3-dihydroxy-2, 3-diaryltetrahydrofurans via N-heterocyclic carbene/base-mediated domino reactions of aromatic aldehydes and vinylselenone. *Org. Lett.* **2017**, *19*, 444−447.

7. For selected examples and recent reviews on NHC catalysis, see: (a) Murauski, K. J. R.; Jaworski, A. A.; Scheidt, K. A. A continuing challenge: N-heterocyclic carbene-catalyzed syntheses of γ-butyrolactones. *Chem. Soc. Rev.* **2018**, *47*, 1773−1782. (b) Menon, R. S.; Biju, A. T.; Nair, V. Recent advances in N-heterocyclic carbene (NHC)-catalysed benzoin reactions. *Beilstein J. Org. Chem.* **2016**, *12*, 444−461. (c) Xu, J.; Yuan, S.; Miao, M. N-Heterocyclic carbene catalyzed [4+ 2] annulation reactions with In Situ generated heterocyclic ortho-quinodimethanes. *Org. Lett.* **2016**, *18*, 3822–3825. (d) Flanigan, D. M.; Romanov-Michailidis, F.; White, N. A.; Rovis, T. Organocatalytic reactions enabled by N-heterocyclic carbenes. *Chem. Rev.* **2015**, *115*, 9307−9387. (e) Mahatthananchai, J.; Bode, J. W. On the mechanism of N-heterocyclic carbene-catalyzed reactions involving acyl azoliums. *Acc. Chem. Res.* **2014**, *47*, 696–707. (f) Patra, A.; Bhunia, A.; Biju, A. T. Facile synthesis of γ-ketophosphonates by an intermolecular Stetter reaction onto vinylphosphonates. *Org. Lett.* **2014**, *16*, 4798–4801. (g) Zhang, J.; Xing, C.; Tiwari, B.; Chi, Y. R. Catalytic activation of carbohydrates as formaldehyde equivalents for Stetter reaction with enones. *J. Am. Chem. Soc.* **2013**, *135*, 8113–8116. (h) Ryan, S. J.; Candish, L.; Lupton, D. W. Acyl anion free N-heterocyclic carbene organocatalysis. *Chem. Soc. Rev.* **2013**, *42*, 4906–4917. (i) De Sarkar, S.; Biswas, A.; Samanta, R. C.; Studer, A. Catalysis with N-Heterocyclic Carbenes under Oxidative Conditions. *Chem. Eur. J.* **2013**, *19*, 4664–4678. (j) Cullen, S. C.; Rovis, T. Catalytic asymmetric Stetter reaction onto vinylphosphine oxides and vinylphosphonates. *Org. Lett.* **2008**, *10*, 3141–3144.

8. For reaction condition, see: Xuan, J.; Feng, Z. J.; Chen, J. R.; Lu, L. Q.; Xiao, W. J. Visible-light-induced C-S bond activation: Facile access to 1,4-diketones from β-ketosulfones. *Eur. J. Org. Chem*. **2014,** *20*, 3045–3049.

9. For reaction condition, see: Fan, X.; He, Y.; Cui, L.; Zhang, X.; Wang, J. Tandem reaction of 1, 2-allenic ketone with α-halo ketone or α-halo ester in water: An efficient and sustainable synthesis of 1,3,4′-tricarbonyl compounds. *Green Chem*. **2011**, *13*, 3218–3223.

10. For reaction condition, see: Che, C., Qian, Z., Wu, M., Zhao, Y., & Zhu, G. Intermolecular oxidative radical addition to aromatic aldehydes: Direct access to 1,4-and 1,5-diketones via silver-catalyzed ring-opening acylation of cyclopropanols and cyclobutanols. *J. Org. Chem.* **2018**, *83*, 5665−5673.

11. For reaction condition, see: Penning, M.; Christoffers, J. Dihydropyridazine derivatives with cyclopenta-, benzo-, furo-, thiopyrano-and pyrido-annulation. *Eur. J. Org. Chem.* **2013**, *2*, 389–400.

12. Chogii, I., Das, P.; Fell, J. S.; Scott, K. A.; Crawford, M. N.; Houk, K. N.; Njardarson, J. T. New class of anion-accelerated amino-Cope rearrangements as gateway to diverse chiral structures. *J. Am. Chem. Soc*. **2017**, *139*, 13141-13146.

13. De Fusco, C.; Fuoco, T.; Croce, G.; Lattanzi, A. Noncovalent organocatalytic synthesis of enantioenriched terminal aziridines with a quaternary stereogenic center. *Org. lett.* **2012,** *14*, 4078-4081.