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Synthesis of β-ketophosphonates via $AgNO_3$-catalyzed hydration of alkynylphosphonates: a rate-enhancement effect of methanol

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ABSTRACT

β-Ketophosphonates were prepared via $AgNO_3$-catalyzed hydration of alkynylphosphonates with a dramatic rate-enhancement effect of methanol. This benign aqueous-methanol method catalyzed by a low-cost catalyst has simple, atom-economical procedure, and was used effectively with a wide range of substrates.

1. Introduction

β-Ketophosphonates represent an important class of carbonyl compounds that are found in a variety of biologically active molecules such as antiinflammatory agents[1] and protein inhibitors.[2] They also act as key building blocks in organic synthesis,[3] especially as intermediates for the synthesis of α,β-unsaturated carbonyl compounds,[4] chiral β-amino[5] and β-hydroxy phosphonic acids.[6] Furthermore, they are prime ligands in organometallic chemistry to control most transition metal catalyzed reactions due to their excellent metal ligation properties.[7]

Due to such wide interest, several β-ketophosphonate syntheses have already been developed and any novel efficient access to provide β-ketophosphonates with good functional group compatibility in high yields would be extraordinarily valuable.[8] Among these developed methods, hydration[9] of alkynylphosphonates catalyzed by transition metals is particularly interesting owning to 100% atom economy and environmental benignity.[10] Mercury salts are originally proposed for such transformation, but high toxicity is a dramatic barrier for applications in both academic and industrial utilization.[8a,8c,8e–g] Palladium salts[8m] and gold(I) complexes[11] are recently explored as catalysts for the reaction. However, these methods suffer from several shortcomings, particularly from the perspective of its applications in commercial syntheses because of the high cost. Surprisingly, silver salts, inexpensive compared to palladium salts and gold(I) complexes, are seldom applied to catalytic hydration of heterosubstituted alkynes.[12] Owing to our continuous interest in the synthesis of α-functionalized carbonyl compounds,[11,13] herein we describe an efficient synthesis of β-ketophosphonates via $AgNO_3$-catalyzed hydration of alkynylphosphonates, which can be easily prepared in one step from commercially readily available terminal alkynes.[14]

2. Results and discussion

Diethyl phenylethynylphosphonate (**1a**) was first chosen as the model substrate to investigate our synthetic approach to β-ketophosphonates. In the presence of 10 mol % of AgCl, the hydration reaction of **1a** was conducted in methanol/water (10/1) mixture[9f,12b,15] at 120 °C. Pleasingly, about 80% GC conversion of **1a** was observed after 24 h (Table 1, entry 1). Attempts to increase the reaction efficiency by varying the silver salts (entries 2–7) revealed that inexpensive $AgNO_3$ was a superior catalyst with a 94% isolated yield (entry 7). Encouraged by the impressive result, we subsequently focused on determining the appropriate solvent (entries 8–17). Only a trace amount of substrate was converted into the corresponding product when the reactions were carried out in water, 1,2-Dichloroethane/H_2O (10/1), CH_3CN/H_2O (10/1) and DMF/H_2O (10/1) (entries 8–11). Switching the solvent to EtOH/H_2O (10/1), *i*PrOH/H_2O (10/1), Ethylene Glycol/H_2O (10/1), 1,3-Propanediol/

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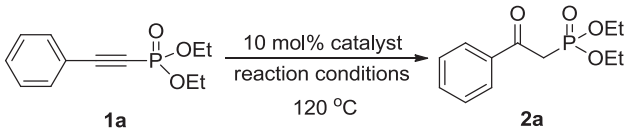
Table 1
Screening optimal conditions[a]



1a 2a

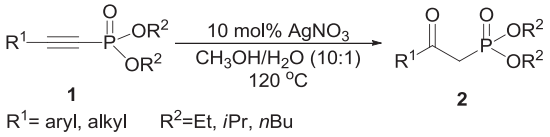
Entry	Catalyst	Reaction condition	Conv.%[b]
1	AgCl	CH_3OH/H_2O(10/1), 120 °C	83
2	$AgBF_4$	CH_3OH/H_2O(10/1), 120 °C	87
3	AgOTf	CH_3OH/H_2O(10/1), 120 °C	92
4	$AgSbF_6$	CH_3OH/H_2O(10/1), 120 °C	85
5	Ag_2SO_4	CH_3OH/H_2O(10/1), 120 °C	83
6	AgOAc	CH_3OH/H_2O(10/1), 120 °C	86
7	$AgNO_3$	CH_3OH/H_2O(10/1), 120 °C	97(94)
8	$AgNO_3$	H_2O, 120 °C	7
9	$AgNO_3$	1,2-Dichloroethane/H_2O(10/1), 120 °C	12
10	$AgNO_3$	CH_3CN/H_2O(10/1), 120 °C	9
11	$AgNO_3$	DMF/H_2O(10/1), 120 °C	11
12	$AgNO_3$	EtOH/H_2O(10/1), 120 °C	48
13	$AgNO_3$	*i*PrOH/H_2O(10/1), 120 °C	27
14	$AgNO_3$	Ethylene Glycol/H_2O(10/1), 120 °C	56
15	$AgNO_3$	1,3-Propanediol/H_2O(10/1), 120 °C	42
16	$AgNO_3$	THF/H_2O(10/1), 120 °C	23
17	$AgNO_3$	Dioxane/H_2O(10/1), 120 °C	34
18[c]	$AgNO_3$	CH_3OH/H_2O(10/1), 120 °C	60
19[d]	$AgNO_3$	CH_3OH/H_2O(10/1), 120 °C	98
20	$AgNO_3$	CH_3OH/H_2O(10/1), 100 °C	89
21	$AgNO_3$	CH_3OH/H_2O(10/1), 80 °C	72
22	$AgNO_3$	CH_3OH/H_2O(10/1), 60 °C	50
23	$Cu(NO_3)_2$	CH_3OH/H_2O(10/1), 120 °C	0
24	$Fe(NO_3)_3$	CH_3OH/H_2O(10/1), 120 °C	0
25	HNO_3	CH_3OH/H_2O(10/1), 120 °C	0

[a] Conditions: **1a** (0.5 mmol), catalyst (10 mol%), solvent (0.5 mL) and water (0.05 mL) in sealed tube at 120 °C for 24 h.
[b] GC conversions are average of at least two runs and the number in parentheses is isolated yield.
[c] 5 mol% $AgNO_3$ was used and the reaction was run for 48 h.
[d] 15 mol% $AgNO_3$ was used and the reaction was finished in 10 h.

H_2O (10/1), THF/H_2O (10/1) and 1,4-Dioxane/H_2O (10/1), the catalytic system provided modest GC conversions (48%, 27%, 56%, 42%, 23% and 34%, respectively, entries 12–17). These results suggested that methanol was essential to dramatically increase of the hydration rates.[15] Less amount of catalyst (5 mol%) took longer time to afford the higher conversion whereas increased amount of catalyst (15 mol%) did not improve the yield (entries 18, 19). Meanwhile, the temperature influenced the reaction significantly. The reaction did become sluggish when the temperature decreased from 120 °C to 60 °C (entries 20–22). The blank experiments showed that the presence of the silver catalyst was necessary in our protocol (entries 23–25).

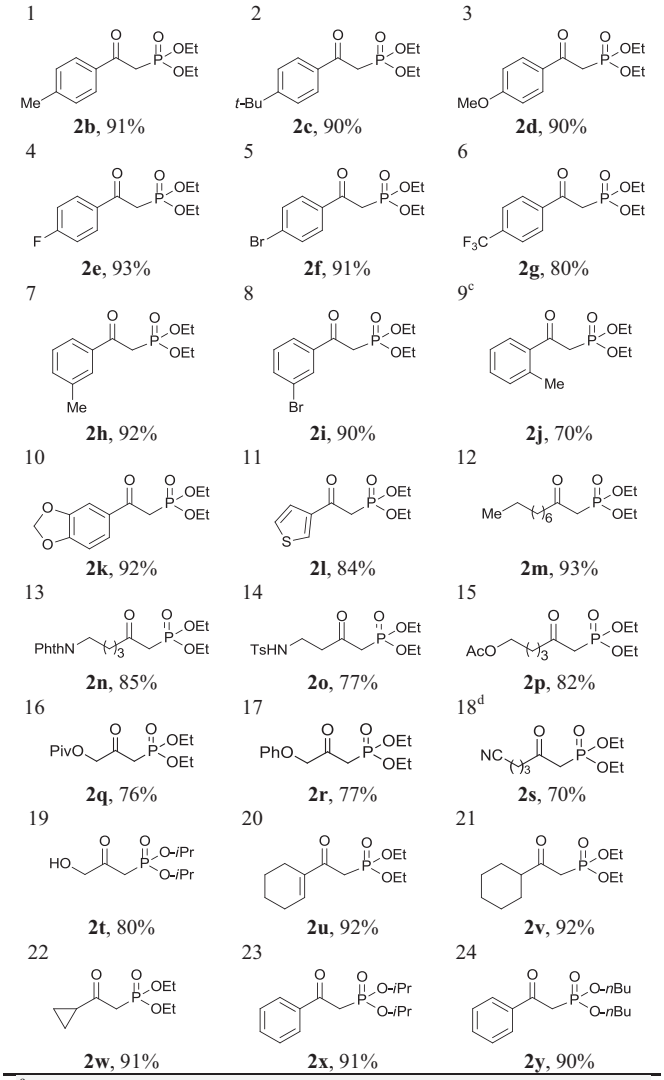
With the optimal conditions in hand (Table 1, entry 7), we embarked on the evaluation of the substrate scope for this transformation. The results were summarized in Table 2. For most cases, the conversions were more than 90%. A variety of aromatic alkynylphosphonates were initially tested. Both electron-donating groups and electron-withdrawing groups at *para* and *meta* positions were all tolerated under the reaction conditions, and excellent yields of the corresponding hydration products were obtained (**2b**–**2i**). These bromide groups were the useful entities amenable to further manipulations by the transition metal-catalyzed cross-coupling strategies. However, the conversion rate of **1j** was slow under the optimal conditions, and 24% of **1j** was still recovered after the reaction was allowed to run for 36 h, likely due to the steric hindrance. Heterocycle-containing alkynylphosphonates (**2k**, **2l**) were also well compatible with this transformation. Moreover, a series of aliphatic alkynylphosphonates were tested. Important functional groups including alkyl (**2m**), phthalimide (PhthNH, **2n**),

Table 2
The reaction scope of alkynylphosphonates[a,b]



1 2

R^1= aryl, alkyl R^2=Et, *i*Pr, *n*Bu

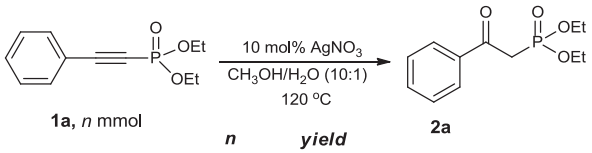


[a] Conditions: alkynylphosphonates (0.5 mmol), $AgNO_3$ (10 mol%), CH_3OH (0.5 mL) and H_2O (0.05 mL) in sealed tube at 120 °C for 24 h.
[b] Isolated yield.
[c] Run for 36 h.
[d] Run for 48 h.

p-toluenesulfonamide ($TsNH_2$, **2o**), acetoxyl (**2p**), pivaloyloxy (PivO, **2q**), phenoxy (**2r**) and cyano moieties (**2s**) were well tolerated under these reaction conditions. However, 24% of substrate remained unreacted even though the reaction time was extended to 48 h in the cases of diethyl (5-cyano-2-oxopentyl)phosphonate (**2s**). We used phosphorus-substituted propargyl alcohol (**1t**) as the substrate and afforded the α-hydroxy product (**2t**) in 80% isolated yield, which highlighted the inexpensive catalytic system and large-scale applications of this product in organic synthesis. There are rarely reported examples concerning on efficient hydration of unprotected propargyl alcohol substrates up to present. Much to our delight, bulky substituents such as cyclohexenyl (**2u**),

cyclohexyl (**2v**) and cyclopropyl (**2w**) groups could proceed successfully. This alkynylphosphonate hydration strategy could also be extended to access the corresponding β-ketophosphonates (**2t**, **2x**, **2y**) when we used other phosphonates as the substrates.

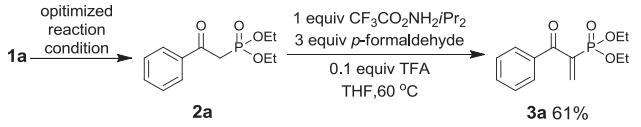
We also explored the reactivity of the $AgNO_3$-catalyzed hydration system for larger-scale synthesis as shown in Scheme 1. The reaction with 3 mmol of diethyl phenylethynylphosphonate produced excellent isolated yield (94%) within 24 h. In the case of 10 mmol scale reaction, 92% of isolated yield was obtained within 36 h. The hydration proceeded smoothly even with a further increased amount of substrate (25 mmol), affording the product in 87% isolated yield. These excellent results showed the promise of the catalytic system for large-scale synthesis in the process of alkynylphosphonates hydration.



n	*yield*
3	*94%, 0.722g*
10	*92%, 2.355g*
25	*87%, 5.568g*

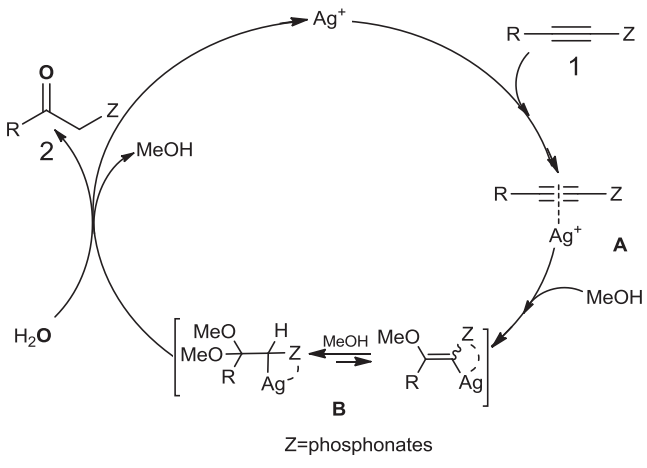
Scheme 1. Large-scale hydration.

This highly efficient synthesis of functionalized β-ketophosphonates permits rapid access to various important phosphonate compounds. For instance, coupled with a subsequent methylenation reaction upon simple workup, this reaction led to diethyl (3-oxo-3-phenylprop-1-en-2-yl)phosphonate in 61% overall yield (Scheme 2).[16]



Scheme 2. Synthesis of diethyl (3-oxo-3-phenylprop-1-en-2-yl)phosphonate.

The possible mechanism was shown in Scheme 3 was proposed on the basis of the previous reported mechanism[9f,12b,17] and our



Scheme 3. Proposed reaction mechanism.

reaction results. First, the silver cation attacked the triple bond of **1** and formed a π-complex **A**, which was subsequently converted to the corresponding σ-complex **B** (enol ether or diketal intermediates)[15] by nucleophilic attack of the methoxy anion. Soon afterwards, the silver complex **B** decomposed to β-ketophosphonate **2** by substitution of the silver atom with a proton in a certain direction. Perhaps the phosphate unit had some stabilization action to the silver, the product formed with high regio- and stereoselectivity.[18]

3. Conclusion

In summary, we have developed a novel and practical method for the synthesis of β-ketophosphonates through $AgNO_3$-catalyzed hydration of alkynylphosphonates with a dramatic rate-enhancement effect of methanol. Considering the readily available substrates and benign aqueous-methanol condition, the inexpensive catalytic system combined with an operationally simple procedure render it a powerful opponent to traditional approaches for the large-scale synthesis of various β-ketophosphonates. Further studies to clearly understand the reaction mechanism and the synthetic applications are ongoing in our laboratory.

4. Experimental section

4.1. General methods and materials

Ethyl acetate (ACS grade), hexanes (ACS grade) were purchased from J&K Scientific Ltd. and used without further purification. Commercially available reagents were used without further purification. Reactions were monitored by TLC. Flash column chromatography was performed over silica gel (200–300 mesh). ^1H NMR and ^{13}C NMR spectra were recorded on a Brucker ARX 400 FT NMR plus spectrometer. High-resolution mass spectra were performed on a Q-TOF microspectrometer.

4.2. General procedure for the synthesis of 2a–2y, 3a

Procedure for 2: To a solution of alkynylphosphonate (0.5 mmol) in CH_3OH (0.5 mL) in sealed tube was added H_2O (0.05 mL) and $AgNO_3$ (0.05 mmol, 8.5 mg), the reaction mixture was stirred at 120 °C and the reaction was monitored by TLC. The reaction typically took 24 h. Upon completion, the mixture was concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (eluent: hexanes/ethyl acetate) to afford **2a**–**2y**.

Procedure for 3a: In a screw capped vial containing freshly distilled THF (3 mL), diethyl (2-oxo-2-phenylethyl)phosphonate (**2a**) (0.3 mmol, 77 mg), *p*-formaldehyde (0.9 mmol, 27 mg) and $CF_3COONH_2iPr_2$ salt (0.3 mmol, 65 mg) were added. CF_3COOH (0.03 mmol, 4 mg) was added and the mixture was warmed to 60 °C and stirred overnight. Upon completion, the mixture was extracted with AcOEt/water and the organic layer dried over Na_2SO_4. The solvent was then removed under reduced pressure. The residue was purified by column chromatography on silica gel (eluent: hexanes/ethyl acetate) to afford **3a**.

4.3. Larger-scale synthesis of 2a

To a solution of Diethyl phenylethynylphosphonate (**1a**) (25 mmol, 5.95 g) in CH_3OH (25 mL) in sealed tube was added H_2O (2.5 mL) and $AgNO_3$ (2.5 mmol, 425 mg), the reaction mixture was stirred at 120 °C for 36 h and the reaction was monitored by TLC. Upon completion, the mixture was concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (eluent: hexanes/ethyl acetate) to afford **2a**.

4.4. Characterization of the compounds

*4.4.1. Diethyl (2-oxo-2-phenylethyl)phosphonate (**2a**).*[8l] Colorless oil (120 mg, 94%); IR(neat): 3065, 2983, 1679, 1598, 1252, 1026, 962 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ=7.98 (d, J=7.2 Hz, 2H), 7.56 (t, J=7.2 Hz, 1H), 7.45 (t, J=7.6 Hz, 2H), 4.12–4.08 (m, 4H), 3.60 (d, $J_{H\text{-}P}$=22.8 Hz, 2H), 1.24 (t, J=7.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=191.81 (d, $J_{C\text{-}P}$=6.5 Hz), 136.31, 133.52, 128.86, 128.44, 62.50 (d, $J_{C\text{-}P}$=6.6 Hz), 38.24 (d, $J_{C\text{-}P}$=129.80 Hz), 16.05 (d, $J_{C\text{-}P}$=6.6 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ=19.97; HRMS (EI): m/z $[M]^+$ calcd for $C_{12}H_{17}O_4P$: 256.0859, found: 256.0861.

*4.4.2. Diethyl (2-oxo-2-(p-tolyl)ethyl)phosphonate (**2b**).*[8i] Colorless oil (123 mg, 91%); IR (neat): 2956, 1684, 1608, 1256, 1028, 986 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ=7.88 (d, J=8.0 Hz, 2H), 7.24 (d, J=8.0 Hz, 2H), 4.14–4.07 (m, 4H), 3.58 (d, $J_{H\text{-}P}$=22.4 Hz, 2H), 2.38 (s, 3H), 1.25 (t, J=7.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=191.34 (d, $J_{C\text{-}P}$=6.5 Hz), 144.49, 133.89, 129.12, 129.02, 62.44 (d, $J_{C\text{-}P}$=6.5 Hz), 38.16 (d, $J_{C\text{-}P}$=129.0 Hz), 21.51, 16.07 (d, $J_{C\text{-}P}$=6.5 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ=20.23; HRMS (EI): m/z $[M]^+$ calcd for $C_{13}H_{19}O_4P$: 270.1015, found: 270.1009.

*4.4.3. Diethyl (2-(4-(tert-butyl)phenyl)-2-oxoethyl)phosphonate (**2c**).* Colorless oil (140 mg, 90%); IR (neat): 2968, 1687, 1586, 1255, 1022, 960 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ=7.90 (d, J=8.4 Hz, 2H), 7.44 (d, J=8.4 Hz, 2H), 4.11–4.05 (m, 4H), 3.57 (d, $J_{H\text{-}P}$=22.8 Hz, 2H), 1.29 (s, 9H), 1.23 (t, J=7.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=191.27 (d, $J_{C\text{-}P}$=6.6 Hz), 157.26, 133.82, 128.82, 125.33, 62.39 (d, $J_{C\text{-}P}$=6.6 Hz), 38.15 (d, $J_{C\text{-}P}$=129.1 Hz), 34.92, 30.79 16.01 (d, $J_{C\text{-}P}$=6.6 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ=20.20; HRMS (EI): m/z $[M]^+$ calcd for $C_{16}H_{25}O_4P$: 312.1485, found: 312.1484.

*4.4.4. Diethyl (2-(4-methoxyphenyl)-2-oxoethyl)phosphonate (**2d**).*[8i] Colorless oil (128 mg, 90%); IR (neat): 2962, 1680, 1594, 1256, 1030, 968 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ=7.98 (d, J=8.8 Hz, 2H), 6.93 (d, J=8.8 Hz, 2H), 4.16–4.09 (m, 4H), 3.86 (s, 3H), 3.57 (d, $J_{H\text{-}P}$=22.8 Hz, 2H), 1.27 (t, $J_{C\text{-}P}$=7.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=190.11 (d, $J_{C\text{-}P}$=6.5 Hz), 163.88, 131.37, 129.51, 113.63, 62.52 (d, $J_{C\text{-}P}$=6.6 Hz), 55.37, 38.08 (d, $J_{C\text{-}P}$=129.1 Hz), 16.10 (d, $J_{C\text{-}P}$=6.6 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ=20.51; HRMS (EI): m/z $[M]^+$ calcd for $C_{13}H_{19}O_5P$: 286.0965, found: 286.0964.

*4.4.5. Diethyl (2-(4-fluorophenyl)-2-oxoethyl)phosphonate (**2e**).* Colorless oil (127 mg, 93%); IR (neat): 2984, 1682, 1603, 1266, 1022, 955 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ=8.02 (dd, J=8.4 Hz, 5.6 Hz, 2H), 7.11 (t, J=8.4 Hz, 2H), 4.14–4.06 (m, 4H), 3.57 (d, $J_{H\text{-}P}$=22.8 Hz, 2H), 1.25 (t, J=7.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=190.18 (d, $J_{C\text{-}P}$=6.6 Hz), 165.91 (d, $J_{C\text{-}F}$=254.4 Hz), 132.77, 131.70 (d, $J_{C\text{-}F}$=9.5 Hz), 115.57 (d, $J_{C\text{-}F}$=21.9 Hz), 62.53 (d, $J_{C\text{-}P}$=6.6 Hz), 38.45 (d, $J_{C\text{-}P}$=128.4 Hz), 16.07 (d, $J_{C\text{-}P}$=5.8 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ=19.58; HRMS (EI): m/z $[M]^+$ calcd for $C_{12}H_{16}FO_4P$: 274.0765, found: 274.0764.

*4.4.6. Diethyl (2-(4-bromophenyl)-2-oxoethyl)phosphonate (**2f**).* Colorless oil (152 mg, 91%); IR (neat): 2958, 1692, 1586, 1253, 1024, 962 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ=7.87 (dd, J=8.4 Hz, 1.2 Hz, 2H), 7.61 (dd, J=8.4 Hz, 1.2 Hz, 2H), 4.14–4.10 (m, 4H), 3.58 (d, $J_{H\text{-}P}$=22.4 Hz, 2H), 1.28 (t, J=7.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=190.83 (d, $J_{C\text{-}P}$=6.6 Hz), 135.14, 131.83, 130.47, 128.95, 62.66 (d, $J_{C\text{-}P}$=6.6 Hz), 38.51 (d, $J_{C\text{-}P}$=128.3 Hz), 16.13 (d, $J_{C\text{-}P}$=6.6 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ=19.37; HRMS (EI): m/z $[M]^+$ calcd for $C_{12}H_{16}BrO_4P$: 333.9964, found: 333.9963.

*4.4.7. Diethyl (2-oxo-2-(4-(trifluoromethyl)phenyl)ethyl)phosphonate (**2g**).* Colorless oil (130 mg, 80%); IR (neat): 2964, 1682, 1253, 1028, 982 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ=8.10 (d, J=8.0 Hz, 2H), 7.70 (d, J=8.0 Hz, 2H), 4.14–4.07 (m, 4H), 3.62 (d, $J_{H\text{-}P}$=23.2 Hz, 2H), 1.25 (t, J=7.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=191.01 (d, $J_{C\text{-}P}$=6.5 Hz), 138.97, 134.69 (q, $J_{C\text{-}F}$=32.8 Hz), 129.31, 125.54 (q, $J_{C\text{-}F}$=3.7 Hz), 122.03, 62.71 (d, $J_{C\text{-}P}$=6.5 Hz), 38.79 (d, $J_{C\text{-}P}$=128.3 Hz), 16.09 (d, $J_{C\text{-}P}$=6.5 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ=18.96; HRMS (EI): m/z $[M]^+$ calcd for $C_{13}H_{16}F_3O_4P$: 324.0733, found: 324.0732.

*4.4.8. Diethyl (2-oxo-2-(m-tolyl)ethyl)phosphonate (**2h**).* Colorless oil (124 mg, 92%); IR (neat): 2958, 1688, 1605, 1250, 1024, 970 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ=7.78–7.76 (m, 2H), 7.37–7.30 (m, 2H), 4.14–4.06 (m, 4H), 3.58 (d, $J_{H\text{-}P}$=22.8 Hz, 2H), 2.38 (s, 3H), 1.24 (t, J=7.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=191.94 (d, $J_{C\text{-}P}$=6.5 Hz), 138.23, 136.41, 134.26, 129.26, 128.30, 126.16, 62.46 (d, $J_{C\text{-}P}$=6.6 Hz), 38.24 (d, $J_{C\text{-}P}$=129.8 Hz), 21.10, 16.03 (d, $J_{C\text{-}P}$=6.6 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ=20.09; HRMS (EI): m/z $[M]^+$ calcd for $C_{13}H_{19}O_4P$: 270.1015, found: 270.1010.

*4.4.9. Diethyl (2-(3-bromophenyl)-2-oxoethyl)phosphonate (**2i**).* Colorless oil (150 mg, 90%); IR (neat): 2945, 1685, 1587, 1253, 1028, 968 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ=8.11 (t, J=2.0 Hz, 1H), 7.93–7.90 (m, 1H), 7.70–7.67 (m, 1H), 7.34 (t, J=8.0 Hz, 1H), 4.15–4.07 (m, 4H), 3.57 (d, $J_{H\text{-}P}$=22.4 Hz, 2H), 1.26 (t, J=7.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=190.61 (d, $J_{C\text{-}P}$=6.5 Hz), 138.14, 136.42, 131.94, 130.15, 127.65, 122.87, 62.74 (d, $J_{C\text{-}P}$=6.5 Hz), 38.64 (d, $J_{C\text{-}P}$=128.3 Hz), 16.17 (d, $J_{C\text{-}P}$=5.8 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ=19.13; HRMS (EI): m/z $[M]^+$ calcd for $C_{12}H_{16}BrO_4P$: 333.9964, found: 333.9958.

*4.4.10. Diethyl (2-oxo-2-(o-tolyl)ethyl)phosphonate (**2j**).* Colorless oil (95 mg, 70%); IR (neat): 3065, 2964, 1678, 1250, 1025, 975 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ=7.67 (d, J=7.2 Hz, 1H), 7.31 (t, J=7.4 Hz, 1H), 7.22–7.16 (dd, J=7.2 Hz, 7.6 Hz, 2H), 4.07–4.00 (m, 4H), 3.52 (d, $J_{H\text{-}P}$=22.4 Hz, 2H), 2.44 (s, 3H), 1.18 (t, J=7.0 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=194.95 (d, $J_{C\text{-}P}$=6.6 Hz), 138.82, 137.10, 131.85, 131.80, 129.48, 125.56, 62.38 (d, $J_{C\text{-}P}$=5.9 Hz), 40.93 (d, $J_{C\text{-}P}$=129.1 Hz), 21.18, 16.10 (d, $J_{C\text{-}P}$=6.6 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ=20.18; HRMS (EI): m/z $[M]^+$ calcd for $C_{13}H_{19}O_4P$: 270.1015, found: 270.1016.

*4.4.11. Diethyl (2-(benzo[d][1,3]dioxol-5-yl)-2-oxoethyl)phosphonate (**2k**).* Colorless oil (138 mg, 92%); IR (neat): 2932, 1685, 1255, 1026, 968 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ=7.60 (d, J=8.4 Hz, 1H), 7.44 (s, 1H), 6.83 (d, J=8.4 Hz, 1H), 6.02 (s, 2H), 4.15–4.07 (m, 4H), 3.53 (d, $J_{H\text{-}P}$=22.8 Hz, 2H), 1.26 (t, J=7.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=189.68 (d, $J_{C\text{-}P}$=6.6 Hz), 152.22, 148.12, 131.26, 125.91, 108.30, 107.69, 101.87, 62.52 (d, $J_{C\text{-}P}$=6.6 Hz), 38.20 (d, $J_{C\text{-}P}$=129.8 Hz), 16.10 (d, $J_{C\text{-}P}$=6.6 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ=20.21; HRMS (EI): m/z $[M]^+$ calcd for $C_{13}H_{17}O_6P$: 300.0757, found: 300.0759.

*4.4.12. Diethyl (2-oxo-2-(thiophen-3-yl)ethyl)phosphonate (**2l**).* Colorless oil (110 mg, 84%); IR (neat): 2960, 1678, 1588, 1246, 1028, 958 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ=8.15 (d, J=2.0 Hz, 1H), 7.51 (d, J=6.0 Hz, 1H), 7.25–7.23 (m, 1H), 4.10–4.03 (m, 4H), 3.46 (d, $J_{H\text{-}P}$=22.8 Hz, 2H), 1.22 (t, J=7.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=185.44 (d, $J_{C\text{-}P}$=6.6 Hz), 141.72, 134.20, 127.12, 126.26, 62.54 (d, $J_{C\text{-}P}$=6.5 Hz), 39.83 (d, $J_{C\text{-}P}$=128.4 Hz), 16.06 (d, $J_{C\text{-}P}$=6.6 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ=19.89; HRMS (EI): m/z $[M]^+$ calcd for $C_{10}H_{15}O_4PS$: 262.0423, found: 262.0420.

*4.4.13. Diethyl (2-oxopentyl)phosphonate (**2m**).* Colorless oil (135 mg, 93%); IR (neat): 2968, 1715, 1258, 1026, 968 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ=4.16–4.08 (m, 4H), 3.04 (d, $J_{H\text{-}P}$=22.4 Hz, 2H), 2.59 (t, J=7.2 Hz, 2H), 1.55 (t, J=7.2 Hz, 2H), 1.33–1.24 (m, 16H), 0.85 (t, J=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=202.20 (d, $J_{C\text{-}P}$=5.9 Hz), 62.42 (d, $J_{C\text{-}P}$=6.5 Hz), 44.03, 42.25 (d, $J_{C\text{-}P}$=126.1 Hz),

31.71, 29.24, 29.02, 28.88, 23.34, 22.54, 16.22 (d, $J_{C\text{-}P}$=6.6 Hz), 13.99; ^{31}P NMR (162 MHz, $CDCl_3$): δ=20.07; HRMS (EI): m/z $[M]^+$ calcd for $C_{14}H_{29}O_4P$: 292.1798, found: 292.1789.

*4.4.14. Diethyl (4-(1,3-dioxoisoindolin-2-yl)-2-oxobutyl)phosphonate (**2n**).* Colorless oil (162 mg, 85%); IR (neat): 2978, 1712, 1485, 1256, 1032, 962 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.82 (dd, J=5.6 Hz, 2.8 Hz, 2H), 7.70 (dd, J=5.6 Hz, 2.8 Hz, 2H), 4.18–4.08 (m, 4H), 3.68 (t, J=6.8 Hz, 2H), 3.06 (d, $J_{H\text{-}P}$=22.8 Hz, 2H), 2.67 (t, J=7.2 Hz, 2H), 1.72–1.59 (m, 4H), 1.32 (t, J=7.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=201.34 (d, $J_{C\text{-}P}$=5.8 Hz), 168.28, 133.81, 131.99, 123.10, 62.50 (d, $J_{C\text{-}P}$=6.5 Hz), 43.10, 42.33 (d, $J_{C\text{-}P}$=126.1 Hz), 37.37, 27.63, 20.38, 16.19 (d, $J_{C\text{-}P}$=5.8 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ=19.89; HRMS (EI): m/z $[M]^+$ calcd for $C_{18}H_{24}NO_6P$: 381.1336, found: 381.1323.

*4.4.15. Diethyl (4-(4-methylphenylsulfonamido)-2-oxobutyl) phosphonate (**2o**).* Colorless oil (145 mg, 77%); IR (neat): 3318, 2946, 1710, 1600, 1258, 1028, 956 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.73 (d, J=8.0 Hz, 2H), 7.30 (d, J=8.4 Hz, 2H), 5.41 (t, J=6.4 Hz, 1H), 4.17–4.09 (m, 4H), 3.14 (q, J=6.0 Hz, 2H), 3.06 (d, $J_{H\text{-}P}$=22.8 Hz, 2H), 2.87 (t, J=5.8 Hz, 2H), 2.42 (s, 3H),1.32 (t, J=7.0 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=201.26 (d, $J_{C\text{-}P}$=6.6 Hz), 143.37, 136.84, 129.70, 126.99, 62.81 (d, $J_{C\text{-}P}$=6.6 Hz), 43.52, 42.55 (d, $J_{C\text{-}P}$=126.1 Hz), 37.90, 21.46, 16.24 (d, $J_{C\text{-}P}$=5.8 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ=19.18; HRMS (EI): m/z $[M]^+$ calcd for $C_{15}H_{24}NO_6PS$: 377.1062, found: 377.1055.

*4.4.16. 4-(Diethoxyphosphoryl)-3-oxobutyl acetate (**2p**).* Colorless oil (120 mg, 82%); IR (neat): 2952, 1718, 1255, 1019, 963 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ=4.09–4.05 (m, 4H), 4.00–3.97 (m, 2H), 3.01 (d, $J_{H\text{-}P}$=23.3 Hz, 2H), 2.60 (t, J=6.4 Hz, 2H), 1.96 (s, 3H), 1.58–1.56 (m, 4H), 1.26 (t, J=7.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=201.29 (d, $J_{C\text{-}P}$=6.6 Hz), 170.87, 63.77, 62.35 (d, $J_{C\text{-}P}$=6.6 Hz), 43.12, 42.25 (d, $J_{C\text{-}P}$=126.8 Hz), 27.58, 20.69, 19.58, 16.06 (d, $J_{C\text{-}P}$=5.8 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ=19.85; HRMS (EI): m/z $[M]^+$ calcd for $C_{12}H_{23}O_6P$: 294.1227, found: 294.1219.

*4.4.17. 3-(Diethoxyphosphoryl)-2-oxopropyl pivalate (**2q**).* Colorless oil (113 mg, 76%); IR (neat): 2976, 1715, 1252, 1025, 956 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ=4.77 (s, 2H), 4.18–4.10 (m, 4H), 3.09 (d, $J_{H\text{-}P}$=22.8 Hz, 2H), 1.33 (t, J=7.2 Hz, 6H), 1.24 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=195.22 (d, $J_{C\text{-}P}$=6.6 Hz), 177.62, 68.08, 62.83 (d, $J_{C\text{-}P}$=5.9 Hz), 39.05 (d, $J_{C\text{-}P}$=128.3 Hz), 38.63, 27.05, 16.22 (d, $J_{C\text{-}P}$=6.6 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ=18.54; HRMS (EI): m/z $[M]^+$ calcd for $C_{12}H_{23}O_6P$: 294.1227, found: 294.1220.

*4.4.18. Diethyl (2-oxo-3-phenoxypropyl)phosphonate (**2r**).* Colorless oil (110 mg, 77%); IR (neat): 2982, 1712, 1248, 1020, 968 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.24–7.20 (m, 2H), 6.92 (t, J=7.4 Hz, 1H), 6.84 (d, J=7.6 Hz, 2H), 4.64 (s, 2H), 4.11–4.05 (m, 4H), 3.21 (d, $J_{H\text{-}P}$=22.4 Hz, 2H), 1.25 (t, J=7.0 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=198.63 (d, $J_{C\text{-}P}$=6.6 Hz), 157.45, 129.61, 121.80, 114.52, 72.63, 62.81 (d, $J_{C\text{-}P}$=6.6 Hz), 38.53 (d, $J_{C\text{-}P}$=127.6 Hz), 16.20 (d, $J_{C\text{-}P}$=5.9 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ=18.83; HRMS (EI): m/z $[M]^+$ calcd for $C_{13}H_{19}O_5P$: 286.0965, found: 286.0962.

*4.4.19. Diethyl (5-cyano-2-oxopentyl)phosphonate (**2s**).* Colorless oil (86 mg, 70%); IR (neat): 2980, 1715, 1252, 1036, 975 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ=4.15–4.07 (m, 4H), 3.06 (d, $J_{H\text{-}P}$=22.4 Hz, 2H), 2.78 (t, J=6.8 Hz, 2H), 2.37 (t, J=7.0 Hz, 2H), 1.93–1.86 (m, 2H), 1.30 (t, J=7.0 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=200.18 (d, $J_{C\text{-}P}$=5.9 Hz), 119.01, 62.59 (d, $J_{C\text{-}P}$=6.5 Hz), 42.31 (d, $J_{C\text{-}P}$=126.1 Hz), 41.49, 19.03, 16.09 (d, $J_{C\text{-}P}$=5.8 Hz), 16.02; ^{31}P NMR (162 MHz, $CDCl_3$): δ=19.40; HRMS (EI): m/z $[M]^+$ calcd for $C_{10}H_{18}NO_4P$: 247.0968, found: 247.0957.

*4.4.20. Diisopropyl (3-hydroxy-2-oxopropyl)phosphonate (**2t**).* Colorless oil (95 mg, 80%); IR (neat): 3375, 2980, 1710, 1235, 1108, 981 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ=4.77–4.69 (m, 2H), 4.33 (s, 2H), 3.16 (d, $J_{H\text{-}P}$=23.2 Hz, 2H), 1.34 (d, J=6.0 Hz, 12H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=202.73(d, $J_{C\text{-}P}$=5.9 Hz), 72.08 (d, $J_{C\text{-}P}$=6.6 Hz), 69.04, 40.28 (d, $J_{C\text{-}P}$=126.1 Hz), 23.89 (d, $J_{C\text{-}P}$=3.7 Hz), 23.77 (d, $J_{C\text{-}P}$=5.1 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ=17.03; HRMS (EI): m/z $[M]^+$ calcd for $C_9H_{19}O_5P$: 238.0965, found: 238.0970.

*4.4.21. Diethyl (2-(cyclohex-1-en-1-yl)-2-oxoethyl)phosphonate (**2u**).* Colorless oil (120 mg, 92%); IR (neat): 2976, 1667, 1260, 1028, 976 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.01 (s, 1H), 4.16–4.09 (m, 4H), 3.31 (d, $J_{H\text{-}P}$=22.8 Hz, 2H), 2.30–2.23 (m, 4H), 1.64–1.59 (m, 4H), 1.31 (t, J=7.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=192.50 (d, $J_{C\text{-}P}$=5.9 Hz), 143.73, 139.22, 62.45 (d, $J_{C\text{-}P}$=6.6 Hz), 36.84 (d, $J_{C\text{-}P}$=130.5 Hz), 26.26, 23.00, 21.70, 21.27, 16.22 (d, $J_{C\text{-}P}$=6.5 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ=21.19; HRMS (EI): m/z $[M]^+$ calcd for $C_{12}H_{21}O_4P$: 260.1172, found: 260.1173.

*4.4.22. Diethyl (2-cyclohexyl-2-oxoethyl)phosphonate (**2v**).* Colorless oil (120 mg, 92%); IR (neat): 2966, 1715, 1258, 1026, 968 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ=4.13–4.06 (m, 4H), 3.07 (d, $J_{H\text{-}P}$=22.4 Hz, 2H), 2.57–2.51 (m, 1H), 1.85–1.83 (m, 2H), 1.75–1.72 (m, 2H), 1.64–1.60 (m, 1H), 1.30–1.18 (m, 11H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=205.22 (d, $J_{C\text{-}P}$=5.8 Hz), 62.30 (d, $J_{C\text{-}P}$=6.6 Hz), 51.24, 40.06 (d, $J_{C\text{-}P}$=127.0 Hz), 28.02, 25.55, 25.30, 16.13 (d, $J_{C\text{-}P}$=6.6 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ=20.44; HRMS (EI): m/z $[M]^+$ calcd for $C_{12}H_{23}O_4P$: 262.1328, found: 262.1330.

*4.4.23. Diethyl (2-cyclopropyl-2-oxoethyl)phosphonate (**2w**).* Colorless oil (100 mg, 91%); IR (neat): 2962, 1718, 1252, 1027, 960 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ=4.12–4.05 (m, 4H), 3.14 (d, $J_{H\text{-}P}$=22.4 Hz, 2H), 2.16–2.09 (m, 1H), 1.27 (t, J=7.2 Hz, 6H), 1.06–1.02 (m, 2H), 0.93–0.88 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=201.94 (d, $J_{C\text{-}P}$=5.9 Hz), 62.29 (d, $J_{C\text{-}P}$=5.8 Hz), 43.04 (d, $J_{C\text{-}P}$=126.9 Hz), 21.49, 16.09 (d, $J_{C\text{-}P}$=6.5 Hz), 11.87; ^{31}P NMR (162 MHz, $CDCl_3$): δ=20.12; HRMS (EI): m/z $[M+H]^+$ calcd for $C_9H_{18}O_4P$: 221.0937, found: 221.0936.

*4.4.24. Diisopropyl (2-oxo-2-phenylethyl)phosphonate (**2x**).*[8m] Colorless oil (129 mg, 91%); IR (neat): 2978, 1677, 1598, 1250, 1102, 975 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.99 (d, J=7.6 Hz, 2H), 7.56 (t, J=7.2 Hz, 1H), 7.45 (t, J=7.6 Hz, 2H), 4.74–4.66 (m, 2H), 3.57 (d, $J_{H\text{-}P}$=22.8 Hz, 2H), 1.26–1.24 (m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=191.99 (d, $J_{C\text{-}P}$=6.6 Hz), 136.60, 133.39, 129.02, 128.38, 71.42 (d, $J_{C\text{-}P}$=6.5 Hz), 39.60 (d, $J_{C\text{-}P}$=129.8 Hz), 23.83 (d, $J_{C\text{-}P}$=3.6 Hz), 23.62 (d, $J_{C\text{-}P}$=5.3 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ=17.71; HRMS (EI): m/z $[M]^+$ calcd for $C_{14}H_{21}O_4P$: 284.1172, found: 284.1168.

*4.4.25. Dibutyl (2-oxo-2-phenylethyl)phosphonate (**2y**).*[8m] Colorless oil (140 mg, 90%); IR (neat): 2965, 1683, 1596, 1269, 1028, 1008 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.98 (d, J=8.4 Hz, 2H), 7.55 (t, J=7.6 Hz, 1H), 7.44 (t, J=7.6 Hz, 2H), 4.05–4.01 (m, 4H), 3.61 (d, $J_{H\text{-}P}$=22.8 Hz, 2H), 1.59–1.52 (m, 4H), 1.34–1.22 (m, 4H), 0.85 (t, J=7.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=191.75 (d, $J_{C\text{-}P}$=6.6 Hz), 136.37, 133.45, 128.87, 128.41, 66.13 (d, $J_{C\text{-}P}$=6.6 Hz), 38.14 (d, $J_{C\text{-}P}$=128.3 Hz), 32.18 (d, $J_{C\text{-}P}$=6.5 Hz), 18.43, 13.37; ^{31}P NMR (162 MHz, $CDCl_3$): δ=19.86; HRMS (EI): m/z $[M]^+$ calcd for $C_{16}H_{25}O_4P$: 312.1485, found: 312.1483.

*4.4.26. Diethyl (3-oxo-3-phenylprop-1-en-2-yl)phosphonate (**3a**).*[16] Colorless oil (52 mg, 65%); ^{1}H NMR (400 MHz, $CDCl_3$):

δ=7.86 (d, J=6.8 Hz, 2H), 7.61–7.57 (m, 1H), 7.49–7.45 (m, 2H), 6.82 (d, $J_{H\text{-}P}$=24.0 Hz, 1H), 6.29 (d, $J_{H\text{-}P}$=44.8 Hz, 1H), 4.22–4.15 (m, 4H), 1.31 (t, J=7.0 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=193.90 (d, $J_{C\text{-}P}$=9.5 Hz), 139.63, 138.47 (d, $J_{C\text{-}P}$=3.6 Hz), 136.13 (d, $J_{C\text{-}P}$=5.1 Hz), 133.58, 129.91, 128.58, 62.91 (d, $J_{C\text{-}P}$=5.8 Hz), 16.27 (d, $J_{C\text{-}P}$=6.6 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ=12.33.

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Supplementary data

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References and notes

1. (a) Whitten, J. P.; Cube, R. V.; Baron, B. M.; McDonald, I. A. *Bioorg. Med. Chem. Lett.* **1993**, *3*, 19; (b) Paterson, I.; Gardner, N. M.; Poullennec, K. G.; Wright, A. E. *Bioorg. Med. Chem. Lett.* **2007**, *17*, 2443; (c) Balg, C.; Blais, S. P.; Bernier, S.; Huot, J. L.; Couture, M.; Lapointe, J.; Chênevert, R. *Biorg. Med. Chem.* **2007**, *15*, 295.
2. (a) Li, X.; Bhandari, A.; Holmes, C. P.; Szardenings, A. K. *Bioorg. Med. Chem. Lett.* **2004**, *14*, 4301; (b) Bernier, S.; Akochy, P.-M.; Lapointe, J.; Chênevert, R. *Biorg. Med. Chem.* **2005**, *13*, 69; (c) Perumal, S. K.; Adediran, S. A.; Pratt, R. F. *Biorg. Med. Chem.* **2008**, *16*, 6987.
3. (a) Mikołajczyk, M.; Zurawiński, R.; Kiełbasiński, P. *Tetrahedron Lett.* **1989**, *30*, 1143; (b) Lentsch, L. M.; Wiemer, D. F. *J. Org. Chem.* **1999**, *64*, 5205; (c) Liu, Y.-L.; Liang, Y.; Pi, S.-F.; Li, J.-H. *J. Org. Chem.* **2009**, *74*, 5691; (d) Zhou, Y.; Yin, S.; Gao, Y.; Zhao, Y.; Goto, M.; Han, L.-B. *Angew. Chem., Int. Ed.* **2010**, *49*, 6852; (e) Kondoh, A.; Yorimitsu, H.; Oshima, K. *Chem. Asian J.* **2010**, *5*, 398; (f) Zhou, Y.; Wang, G.; Saga, Y.; Shen, R.; Goto, M.; Zhao, Y.; Han, L.-B. *J. Org. Chem.* **2010**, *75*, 7924; (g) Pei, C.-K.; Wu, L.; Lian, Z.; Shi, M. *Org. Biomol. Chem.* **2012**, *10*, 171; (h) Li, Y.; Das, S.; Zhou, S.; Junge, K.; Beller, M. *J. Am. Chem. Soc.* **2012**, *134*, 9727; (i) Debrouwer, W.; Heugebaert, T. S. A.; Van Hecke, K.; Stevens, C. V. *J. Org. Chem.* **2013**, *78*, 8232; (j) Essid, I.; Touil, S. *ARKIVOC* **2013**, *4*, 98; (k) Radwan-Olszewska, K.; Palacios, F.; Kafarski, P. *J. Org. Chem.* **2011**, *76*, 1170.
4. (a) Maryanoff, B. E.; Reitz, A. B. *Chem. Rev.* **1989**, *89*, 863; (b) Pronin, S. V.; Martinez, A.; Kuznedelov, K.; Severinov, K.; Shuman, H. A.; Kozmin, S. A. *J. Am. Chem. Soc.* **2011**, *133*, 12172; (c) Müller, S.; Mayer, T.; Sasse, F.; Maier, M. E. *Org. Lett.* **2011**, *13*, 3940; (d) Hashmi, A. S. K.; Wang, T.; Shi, S.; Rudolph, M. *J. Org. Chem.* **2012**, *77*, 7761; (e) Yang, W.; Yu, Y.; Zhang, T.; Hansmann, M. M.; Pflästerer, D.; Hashmi, A. S. K. *Adv. Synth. Catal.* **2013**, *355*, 2037.
5. Ryglowski, A.; Kafarski, P. *Tetrahedron* **1996**, *52*, 10685.
6. (a) Kitamura, M.; Tokunaga, M.; Noyori, R. *J. Am. Chem. Soc.* **1995**, *117*, 2931; (b) Chávez, M. Á.; Vargas, S.; Suárez, A.; Álvarez, E.; Pizzano, A. *Adv. Synth. Catal.* **2011**, *353*, 2775; (c) Tao, X.; Li, W.; Ma, X.; Li, X.; Fan, W.; Zhu, L.; Xie, X.; Zhang, Z. *J. Org. Chem.* **2012**, *77*, 8401.
7. (a) Cotton, F. A.; Schunn, R. A. *J. Am. Chem. Soc.* **1963**, *85*, 2394; (b) McCabe, D. J.; Duesler, E. N.; Paine, R. T. *Inorg. Chem.* **1985**, *24*, 4626; (c) Salles, L.; Nixon, A. F.; Russell, N. C.; Clarke, R.; Pogorzelec, P.; Cole-Hamilton, D. J. *Tetrahedron: Asymmetry* **1999**, *10*, 1471; (d) Koprowski, M.; Szymańska, D.; Bodzioch, A.; Marciniak, B.; Różycka-Sokołowska, E.; Bałczewski, P. *Tetrahedron* **2009**, *65*, 4017.
8. (a) Sturtz, G.; Charrier, C.; Normant, H. *Bull. Soc. Chim. Fr.* **1966**, 1707; (b) Chattha, M. S.; Aguiar, A. M. *J. Org. Chem.* **1973**, *38*, 2908; (c) Peiffer, G.; Courbis, P. *Can. J. Chem.* **1974**, *52*, 2894; (d) Calogeropoulou, T.; Hammond, G. B.; Wiemer, D. F. *J. Org. Chem.* **1987**, *52*, 4185; (e) Poss, A. J.; Belter, R. K. *J. Org. Chem.* **1987**, *52*, 4810; (f) Corey, E. J.; Virgil, S. C. *J. Am. Chem. Soc.* **1990**, *112*, 6429; (g) Guile, S. D.; Saxton, J. E.; Thornton-Pett, M. *J. Chem. Soc., Perkin Trans. 1* **1992**, 1763; (h) Baker, T. J.; Wiemer, D. F. *J. Org. Chem.* **1998**, *63*, 2613; (i) Luke, G. P.; Seekamp, C. K.; Wang, Z.-Q.; Chenard, B. L. *J. Org. Chem.* **2008**, *73*, 6397; (j) Maloney, K. M.; Chung, J. Y. L. *J. Org. Chem.* **2009**, *74*, 7574; (k) Milburn, R. R.; McRae, K.; Chan, J.; Tedrow, J.; Larsen, R.; Faul, M. *Tetrahedron Lett.* **2009**, *50*, 870; (l) Wei, W.; Ji, J.-X. *Angew. Chem., Int. Ed.* **2011**, *50*, 9097; (m) Li, X.; Hu, G.; Luo, P.; Tang, G.; Gao, Y.; Xu, P.; Zhao, Y. *Adv. Synth. Catal.* **2012**, *354*, 2427.
9. (a) Fukuda, Y.; Utimoto, K. *J. Org. Chem.* **1991**, *56*, 3729; (b) Baidossi, W.; Lahav, M.; Blum, J. *J. Org. Chem.* **1997**, *62*, 669; (c) Suzuki, T.; Tokunaga, M.; Wakatsuki, Y. *Org. Lett.* **2001**, *3*, 735; (d) Tokunaga, M.; Suzuki, T.; Koga, N.; Fukushima, T.; Horiuchi, A.; Wakatsuki, Y. *J. Am. Chem. Soc.* **2001**, *123*, 11917; (e) Nishizawa, M.; Skwarczynski, M.; Imagawa, H.; Sugihara, T. *Chem. Lett.* **2002**, *31*, 12; (f) Mizushima, E.; Sato, K.; Hayashi, T.; Tanaka, M. *Angew. Chem., Int. Ed.* **2002**, *41*, 4563; (g) Grotjahn, D. B.; Lev, D. A. *J. Am. Chem. Soc.* **2004**, *126*, 12232; (h) Sanz, S.; Jones, L. A.; Mohr, F.; Laguna, M. *Organometallics* **2007**, *26*, 952; (i) Ackermann, L.; Kaspar, L. T. *J. Org. Chem.* **2007**, *72*, 6149; (j) Marion, N.; Ramón, R. n. S.; Nolan, S. P. *J. Am. Chem. Soc.* **2009**, *131*, 448; (k) Wu, X.-F.; Bezier, D.; Darcel, C. *Adv. Synth. Catal.* **2009**, *351*, 367; (l) Nun, P.; Ramón, R. S.; Gaillard, S.; Nolan, S. P. *J. Organomet. Chem.* **2011**, *696*, 7; (m) Nun, P.; Dupuy, S.; Gaillard, S.; Poater, A.; Cavallo, L.; Nolan, S. P. *Catal. Sci. Technol.* **2011**, *1*, 58; (n) Wong, W.-L.; Ho, K.-P.; Lee, L. Y. S.; Lam, K.-M.; Zhou, Z.-Y.; Chan, T. H.; Wong, K.-Y. *ACS Catal.* **2011**, *1*, 116; (o) Mukherjee, A.; Liu, R.-S. *Org. Lett.* **2011**, *13*, 660; (p) Czégéni, C. E.; Papp, G.; Kathó, Á.; Joó, F. J. *Mol. Catal. A: Chem.* **2011**, *340*, 1; (q) Tachinami, T.; Nishimura, T.; Ushimaru, R.; Noyori, R.; Naka, H. *J. Am. Chem. Soc.* **2013**, *135*, 50; (r) Trentin, F.; Chapman, A. M.; Scarso, A.; Sgarbossa, P.; Michelin, R. A.; Strukul, G.; Wass, D. F. *Adv. Synth. Catal.* **2012**, *354*, 1095; (s) Cabrero-Antonino, J. R.; Leyva-Pérez, A.; Corma, A. *Chem.—Eur. J.* **2012**, *18*, 11107; (t) Gao, Q.; Li, S.; Pan, Y.; Xu, Y.; Wang, H. *Tetrahedron* **2013**, *69*, 3775.
10. (a) Beller, M.; Seayad, J.; Tillack, A.; Jiao, H. *Angew. Chem., Int. Ed.* **2004**, *43*, 3368; (b) Hintermann, L.; Labonne, A. *Synthesis* **2007**, 1121.
11. Xie, L.; Yuan, R.; Wang, R.; Peng, Z.; Xiang, J.; He, W. *Eur. J. Org. Chem.* **2014**, *2014*, 2668.
12. (a) Das, R.; Chakraborty, D. *Appl. Organomet. Chem.* **2012**, *26*, 722; (b) Thuong, M. B. T.; Mann, A.; Wagner, A. *Chem. Commun.* **2012**, 434; (c) Chen, Z.-W.; Ye, D.-N.; Qian, Y.-P.; Ye, M.; Liu, L.-X. *Tetrahedron* **2013**, *69*, 6116; (d) Venkateswara Rao, K. T.; Sai Prasad, P. S.; Lingaiah, N. *Green. Chem.* **2012**, *14*, 1507.
13. (a) Ye, L.; He, W.; Zhang, L. *J. Am. Chem. Soc.* **2010**, *132*, 8550; (b) He, W.; Li, C.; Zhang, L. *J. Am. Chem. Soc.* **2011**, *133*, 8482; (c) Ye, L.; He, W.; Zhang, L. *Angew. Chem., Int. Ed.* **2011**, *50*, 3236; (d) He, W.; Xie, L.; Xu, Y.; Xiang, J.; Zhang, L. *Org. Biomol. Chem.* **2012**, *10*, 3168; (e) Wu, C.; Huang, W.; He, W.; Xiang, J. *Chem. Lett.* **2013**, *42*, 1233; (f) Wu, C.; Liang, Z.; Yan, D.; He, W.; Xiang, J. *Synthesis* **2013**, *45*, 2605; (g) Wu, C.; Liang, Z.-W.; Xu, Y.-Y.; He, W.-M.; Xiang, J.-N. *Chin. Chem. Lett.* **2013**, *24*, 1064; (h) Xie, L.; Liang, Z.; Yan, D.; He, W.; Xiang, J. *Synlett* **2013**, 1809; (i) Xie, L.; Wu, Y.; Yi, W.; Zhu, L.; Xiang, J.; He, W. *J. Org. Chem.* **2013**, *78*, 9190; (j) Huang, W.; Xiang, J.; He, W. *Chem. Lett.* **2014**, *43*, 893; (k) Xiang, J.; Yuan, R.; Wang, R.; Yi, N.; Lu, L.; Zou, H.; He, W. *J. Org. Chem.* **2014**, *79*, 11378–11382.
14. (a) Gao, Y.; Wang, G.; Chen, L.; Xu, P.; Zhao, Y.; Zhou, Y.; Han, L.-B. *J. Am. Chem. Soc.* **2009**, *131*, 7956; (b) Qu, Z.; Chen, X.; Yuan, J.; Qu, L.; Li, X.; Wang, F.; Ding, X.; Zhao, Y. *Can. J. Chem.* **2012**, *90*, 747.
15. Leyva, A.; Corma, A. *J. Org. Chem.* **2009**, *74*, 2067.
16. De Fusco, C.; Fuoco, T.; Croce, G.; Lattanzi, A. *Org. Lett.* **2012**, *14*, 4078.
17. (a) Teles, J. H.; Brode, S.; Chabanas, M. *Angew. Chem., Int. Ed.* **1998**, *37*, 1415; (b) Oonishi, Y.; Gómez-Suárez, A.; Martin, A. R.; Nolan, S. P. *Angew. Chem., Int. Ed.* **2013**, *52*, 9767.
18. Chen, Z.; Li, J.; Jiang, H.; Zhu, S.; Li, Y.; Qi, C. *Org. Lett.* **2010**, *12*, 3262.