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Graphical Abstract

Acetonitrile-dependent oxyphosphorylation: a mild one-pot synthesis of β-ketophosphonates from alkenyl acids or alkenes

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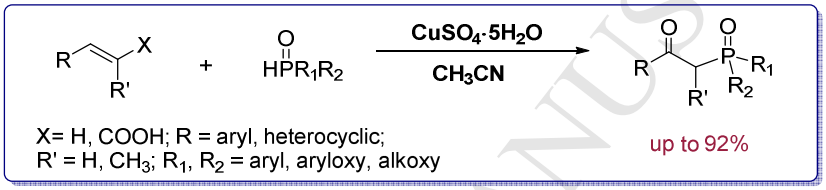

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ABSTRACT

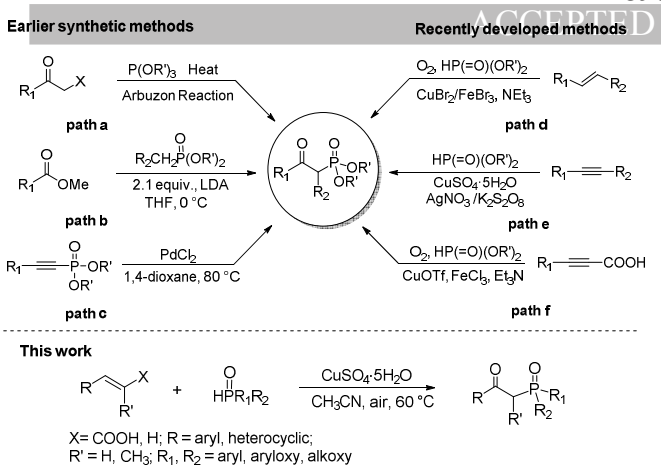
An efficient one-pot synthesis of β-ketophosphonates has been developed, via the reaction of α,β-alkenyl carboxylic acids or alkenes with *H*-phosphonates and air oxygen, catalyzed by $CuSO_4 \cdot 5H_2O$ in CH_3CN. CH_3CN plays a decisive role, probably by forming an active oxygen complex $[(MeCN)_nCu^{II}\text{-}O\text{-}O\cdot]$.

1. Introduction

Active-oxygen species generated on a copper complex has long been a hot research not only in chemistry but also in physiology and biology, since it has close relevance to oxidation reactions in biological as well as synthetic and catalytic processes.[1] A great deal of efforts has thus made in recent years to develop specific copper ligands, enabling stabilizing such reactive active-oxygen complex in synthetic studies.[2] Even though it is well known that acetonitrile is an excellent ligand for copper (II) ion, it is pity that oxidation reactions participated by copper (II)-acetonitrile complex have been reported rarely.[3] It remains challenging to develop efficient aerobic oxidation systems participated by copper (II)-acetonitrile complex.

β-Ketophosphonates are versatile intermediates for various synthetically useful transformations,[4] especially for the construction of alkenes through the well known Horner-Wadsworth-Emmons (HWE) reaction.[5] β-Ketophosphonates also exhibit interesting bioactivities and prominent metal-complexing abilities.[6] They have been successfully applied as extractants for transition elements, lanthanides, actinoid and alkali metals etc.[7] Great efforts have been made during the past several decades to synthesize β-ketophosphonate scaffolds. Earlier synthetic methods mainly include Arbuzov reaction (Scheme 1, path a),[8] acylation of alkylphosphonates under strong basic or acidic reaction conditions (Scheme 1, path b),[9] and hydration of alkynylphosphonates catalyzed by palladium (II) and gold (I) catalysts (Scheme 1, path c).[10] However, nearly all those earlier developed methods suffer from inaccessible materials, and moreover, for some reactions, expensive catalysts, or harsh basic or acidic reaction conditions are required. Thus, more benign, efficient and atom-economic synthetic strategies have been pursued aggressively over the past few years.

In 2011, Ji's group opened up a new route to access β-ketophosphonates by reacting easily available alkenes with dioxygen and *H*-phosphonates in the presence of Cu-Fe cocatalysts (Scheme 1, path d).[11] In 2015, our group created an elegant synthesis of β-ketophosphonates from alkynes and dialkyl *H*-phosphonates in the presence of $AgNO_3/CuSO_4$ and $K_2S_2O_8$ (Scheme 1, path e).[12] The other synthetic methods concerning direct oxyphosphorylation of alkynes with *H*-phosphonates were subsequently reported by He's group and Song's group, respectively.[13] Over the past few years, the use of both α,β-alkynyl carboxylic acids and α,β-alkenyl carboxylic acids, synthetically as terminal alkyne and alkene equivalents, began to be reported in the literature.[14] Direct use of α,β-alkynyl carboxylic acids and α,β-alkenyl carboxylic acids has some advantages, such as no unpleasant smell, easy handling and storage due they are solids.[14a] It is worth mentioning here that, α,β-alkenyl carboxylic acids are generally more cheaper than corresponding α,β-alkynyl carboxylic acids. Thus, exploration of new synthetic methods for β-ketophosphonates with α,β-alkenyl carboxylic acids would be preferentially encouraged. Song's group very recently put forward synthetic strategies to reach β-ketophosphonates, in which $CuOTf/FeCl_3$-cocatalysts were used to activate the decarboxylation-oxyphosphorylation reaction of



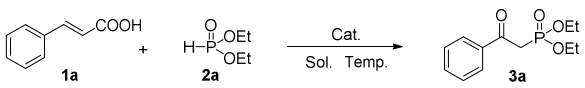
Scheme 1. Comparison of previous methods with this work

alkenyl or alkynyl carboxylic acids with *H*-phosphonates (Scheme 1, path f).[13a] Herein, we disclose a simpler synthetic strategy, by which a variety of β-ketophosphonates were synthesized efficiently by the reaction of α,β-alkenyl carboxylic acids or alkenes with *H*-phosphonates and air oxygen, catalyzed by $CuSO_4 \cdot 5H_2O$ in CH_3CN under open air conditions. In a sharp contrast to Song's method, the most prominent advantage of our reaction is using common and inexpensive $CuSO_4 \cdot 5H_2O$, instead of using much more expensive CuOTf as a catalyst. The advantages also include a base-free condition and a wide reaction scope. The scope of the reaction encompasses both alkenyl carboxylic acids and alkenes, being suitable for transformation of not only alkenyl carboxylic acids but also alkenes into the corresponding β-ketophosphonates.

2. Results and discussion

We initiated the important study, starting with establishing optimal experimental conditions using the model reaction of cinnamic acid (**1a**) with diethyl phosphite (**2a**) under open-air conditions, as summarized in Table 1. The solvent system employed sometimes notably affect the reaction efficiency. The effect of solvents on the model reaction was first investigated by reacting **1a** with 2 equiv. of **2a** in various solvent in the presence of $CuSO_4 \cdot 5H_2O$ (10 mol %) at 60 °C for 6 h (Table 1. entries 1-8). Astonishingly, conducting the reaction in any solvents like THF, DCE, DMF, 1,4-dioxane, EtOH, EtOAc and DMSO, did not bring about any product of **3a** (entries 1-7), but in only CH_3CN, the reaction proceeded smoothly, affording **3a** in 74% yield (entry 8). This abnormal solvent effect phenomenon puzzled us and encouraged us to explore the deep reason behind the result shortly afterwards. The effects of some common metal salt catalysts on the reaction were then investigated, as summarized in entries 8-16. CuCl, $CoCl_2 \cdot 6H_2O$ and $NiCl_2 \cdot 6H_2O$ exhibited no any catalytic activity for the model reaction (entries 12, 14 and 15). $Cu(OAc)_2 \cdot H_2O$ and $FeCl_3 \cdot 6H_2O$ afforded only trace product of **3a**, which was detected by ^{31}P NMR (entries 11, 13). Comparatively, $Cu(NO_3)_2 \cdot 3H_2O$ and Ag_2CO_3 gave about 48% and 39% yields of product, respectively (entries 10, 16). Anhydrous cupric sulfate $CuSO_4$ (entry 9) gave a little low yield of **3a** (74%) than that of $CuSO_4 \cdot 5H_2O$ (entry 8). Thus, $CuSO_4 \cdot 5H_2O$, the cheapescopper salt, was still the best one among metal salt catalysts tested (entry 8).The investigation on the amount of $CuSO_4 \cdot 5H_2O$ (entries 8, 17-18) indicated that 10 mol% was still the most appropriate amount of the catalysts. Then the influence of temperature on the model reaction was investigated (entries 8, 19-21). It can be seen that the 60 °C is the most appropriate temperature, among the tested temperature

Table 1. Optimization of the reaction parameters[a,b]

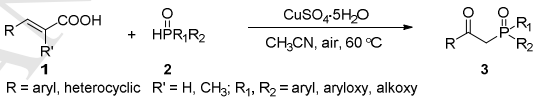


1a + 2a → 3a

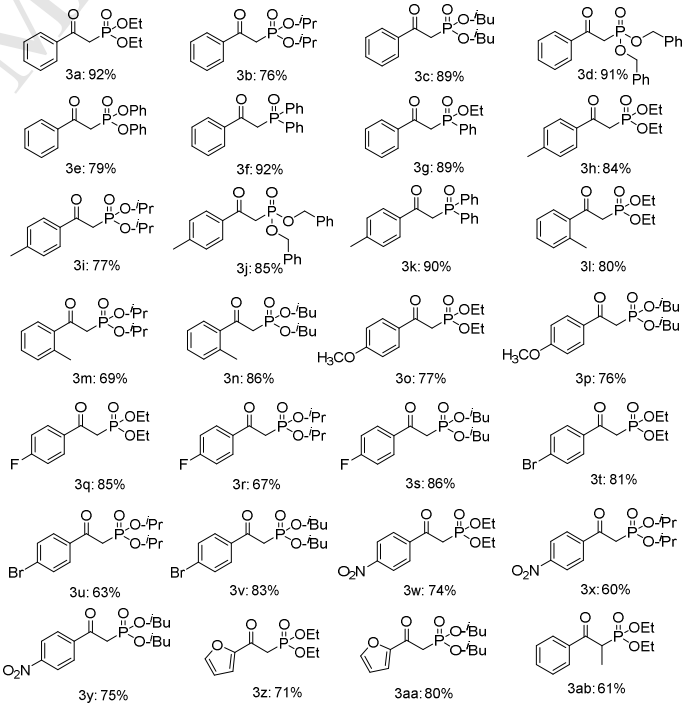
Entry	Catalyst (mol%)	2a (equiv)	Temperture	Solvent	Yield (%)[b]
1	$CuSO_4 \cdot 5H_2O$ (10)	1.5	60	THF	NR
2	$CuSO_4 \cdot 5H_2O$ (10)	1.5	60	DCE	NR
3	$CuSO_4 \cdot 5H_2O$ (10)	1.5	60	DMF	NR
4	$CuSO_4 \cdot 5H_2O$ (10)	1.5	60	1,4-dioxane	NR
5	$CuSO_4 \cdot 5H_2O$ (10)	1.5	60	EtOH	NR
6	$CuSO_4 \cdot 5H_2O$ (10)	1.5	60	EtOAc	NR
7	$CuSO_4 \cdot 5H_2O$ (10)	1.5	60	DMSO	ND
8	$CuSO_4 \cdot 5H_2O$ (10)	1.5	60	CH_3CN	74
9	$CuSO_4$ (10)	1.5	60	CH_3CN	71
10	$Cu(NO_3)_2 \cdot 3H_2O$ (10)	1.5	60	CH_3CN	48
11	$Cu(OAc)_2 \cdot H_2O$ (10)	1.5	60	CH_3CN	trace
12	CuCl (10)	1.5	60	CH_3CN	NR
13	$FeCl_3 \cdot 6H_2O$ (10)	1.5	60	CH_3CN	trace
14	$CoCl_2 \cdot 6H_2O$ (10)	1.5	60	CH_3CN	NR
15	$NiCl_2 \cdot 6H_2O$ (10)	1.5	60	CH_3CN	NR
16	Ag_2CO_3 (10)	1.5	60	CH_3CN	39
17	$CuSO_4 \cdot 5H_2O$(5)	1.5	60	CH_3CN	68
18	$CuSO_4 \cdot 5H_2O$(15)	1.5	60	CH_3CN	72
19	$CuSO_4 \cdot 5H_2O$(10)	1.5	40	CH_3CN	57
20	$CuSO_4 \cdot 5H_2O$(10)	1.5	50	CH_3CN	68
21	$CuSO_4 \cdot 5H_2O$(10)	1.5	70	CH_3CN	74
22	$CuSO_4 \cdot 5H_2O$(10)	1.0	60	CH_3CN	55
23	**$CuSO_4 \cdot 5H_2O$(10)**	**2.0**	**60**	**CH_3CN**	**92**
24	$CuSO_4 \cdot 5H_2O$(10)	2.5	60	CH_3CN	90

[a] Reaction conditions: 0.2 mmol of **1a**, and 4 mL of solvent in a 25 mL round bottom flask for 6 h. [b] Isolated yields. NR = no reaction ND = no detected

Table 2. Scope of the oxyphosphorylation of alkenyl acids[a,b]



1 + 2 → 3



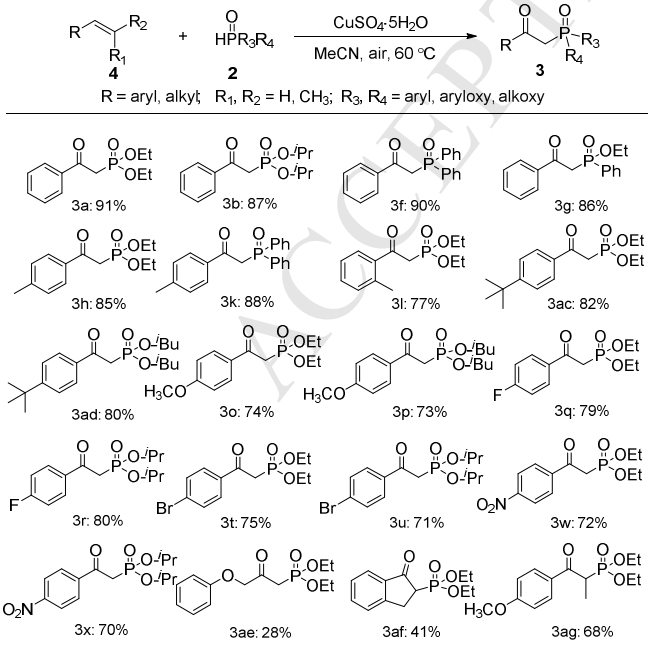
[a] Reaction conditions: 0.2 mmol of **1**, 0.4 mmol of **2**, $CuSO_4 \cdot 5H_2O$ (10 mol%) and 4 mL of CH_3CN in a 25 mL round bottom flask at 60 °C for 6 h. [b] Isolated yields.

regions 40-70 °C. At last, the ideal amount of diethyl phosphite was explored (entries 8, 22-24). The result indicates that 2.0 equiv. is the best choice. Therefore, the best yield of **3a** was obtained by employing 10 mol% $CuSO_4 \cdot 5H_2O$ and 2.0 equivalents of diethyl phosphite in CH_3CN at 60 °C for 6 h (entry 23).

With the optimized conditions in hand, we began to examine the generality and the substrate scope of this synthetic strategy, as demonstrated in Table 2. As it can be seen, a series of dialkyl *H*-phosphonates, including diethyl phosphite, diisopropyl, diisobutyl, dibenzyl, and diphenyl phosphates, reacted well with cinnamic acid itself, affording the corresponding β-ketophosphonates **3a-e** in good to excellent yields (Table 2). Much to our delight, diphenylphosphine oxide and ethyl phenylphosphinate, two other kinds of important organophosphorous reagents, were found to be well compatible for the decarboxylation-oxyphosphorylation reaction, leading to the desired products **3f** and **3g** in excellent yields, respectively. Meanwhile, a large variety of substituted phenylacrylic acid, bearing both electron-donating groups (Me, OCH_3) and electron-withdrawing groups (F, Br, NO_2) on the phenyl ring, reacted smoothly with various organophosphorus reagents, affording the corresponding target products in good to excellent yields (**3h-y**). It can be seen here that the electronic effects of the substituents attached to phenyl rings had no noticeable influence on the efficiency of decarboxylation-oxyphosphorylation reactions. Furthermore, (E)-3-(furan-2-yl)acrylic acid, a heteroaromatic alkenyl carboxylic acids, as well as (E)-2-methyl-3-phenylacrylic acid, a α-substituted alkenyl carboxylic acids, reacted well with dialkyl *H*-phosphonates, giving **3z, 3aa-b** in good yields, respectively.

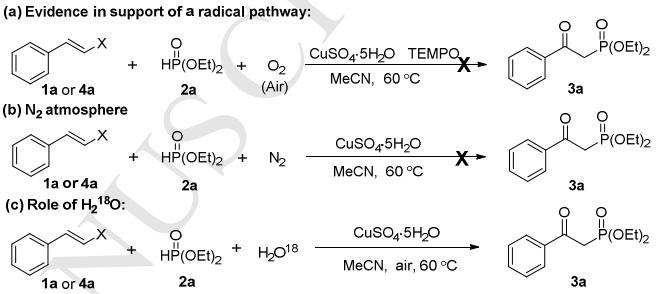
The methodology covered much more wide range of reactants than we expected. Alkenes, commonly employed as readily available building blocks for a wide variety of reactions, to our surprise, were well compatible for the oxyphosphorylation reaction as well. Styrene was initially selected to submit to the reaction conditions. Further optimization of reaction condition indicated that the corresponding β-ketophosphonates could be obtained in excellent yield using relatively less amount of *H*-phosphonate within much reduced time (for details see Supplementary Material Table S1). Subsequently, a large variety of alkenes and *H*-phosphonates were employed to explore the scope of the reaction (Table 3). All the organophosphorus reagents mentioned above, as well as a large variety of alkenes were all compatible well for the oxyphosphorylation reaction. To our delight, 1*H*-indene and (Z)-1-methoxy-4-(prop-1-en-1-yl)benzene, two internal alkenes, reacted smoothly with diethyl phosphite, affording the corresponding β-ketophosphonates **3af** and **3ag** in moderate yields.

Table 3. Scope of the oxyphosphorylation of alkenes[a,b]

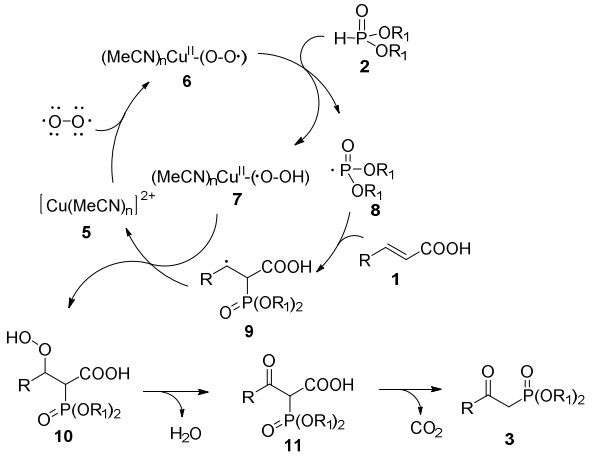


[a] Reaction conditions: 0.2 mmol of **4**, 0.3mmol of **2**, $CuSO_4 \cdot 5H_2O$ (10 mol%) and 4 mL of CH_3CN in a 25 mL round bottom flask at 60 °C for 3 h. [b] Isolated yields.

Next, we carried out three more experiments to explore the related reaction mechanism (Scheme 2). When TEMPO (2,2,6,6-tetramethyl-l-piperidinyloxy), a widely used radical scavenger, was added into the reaction mixture, the reaction was found to be completely restrained, suggesting that radical processes might be involved (Scheme 2a). When the reaction was carried out under a nitrogen atmosphere, no desire product was obtained, indicating that the presence of oxygen is indispensable (Scheme 2b). Then an isotope labeling study was conducted. In the presence of $H_2{}^{18}O$, no corresponding isotope-labeled β-ketophosphonate was detected by high-resolution ESI-MS (Scheme 2c), implying that carbonyl oxygen in the product should originally be from oxygen in air.



Scheme 2. Additional studies for mechanism. Reaction conditions: X = COOH, 0.2 mmol of **1a**, 0.4 mmol of **2a**, $CuSO_4 \cdot 5H_2O$ (10 mol%), and 4 mL of CH_3CN at 60 °C for 6 h. X = H, 0.2 mmol of **4a**, 0.3mmol of **2a**, $CuSO_4 \cdot 5H_2O$ (10 mol%), and 4 mL of in CH_3CN at 60 °C for 3 h. (a) TEMPO (4 equiv.) under air (b) nitrogen ball (c) $H_2{}^{18}O$ (1 equiv.)



Scheme 3. Proposed reaction mechanism

A plausible mechanism for the decarboxylation-oxyphosphorylation reaction is thus proposed accordingly as indicated in Scheme 3. It is well known that copper(II) ion easily forms acetonitrile-soluble complex $[Cu(MeCN)_n]^{2+}$.[15] In this case, complex $[Cu(MeCN)_n]^{2+}$ **5** is an indispensable initiator for the subsequent cascade of the decarboxylation-oxyphosphorylation reaction. As reported by many literatures, copper-active-oxygen proteins play essential roles in oxygen transport in biological systems, being one of the hot researches of biochemistry.[16] Copper-active-oxygen complexes are also key intermediates involved in a variety of Cu-catalyzed-aerobic oxidation reactions.[17] It is well known that molecular oxygen is a diradical

in the ground state with one unpaired electron on each oxygen. Here O_2 in air reacts further with copper(II)-acetonitrile complex **5**, giving copper-active-oxygen complex **6**, which then quickly attacks dialkyl *H*-phosphonate **2**, forming hydroperoxide complex **7** as well as phosphonyl radical **8**. The resulting radical **8** regioselectively adds to α,β-alkenyl carboxylic acid **1**, leading to the formation of radical **9**. Radical **9** continuously reacts with hydroperoxide complex **7** to produce hydroperoxide intermediate **10**, and meanwhile, complex $[Cu(MeCN)_n]^{2+}$ **5** is regenerated. Afterwards, intermediate **10** dehydrates to produce compound **11**. Subsequently, an energetically favorable decarboxylation of compound **11** is followed, leading to the formation of target β-ketophosphonate **3**. A similar mechanism concerning using alkenes as reactants to synthesize the related β-ketophosphonates can be found in Supplementary Material Scheme S2 in details.

3. Conclusion

In conclusion, a relatively simple synthetic strategy has been developed, by which a large variety of β-ketophosphonates were synthesized smoothly by the reaction of α,β-alkenyl carboxylic acids or alkenes with *H*-phosphonates, catalyzed by $CuSO_4 \cdot 5H_2O$ in CH_3CN under open air conditions. Molecular oxygen (O_2) is prerequisite for achieving the meaningful synthesis of β-ketophosphonates. Oxygen (O_2) in air is initially trapped by $[Cu(MeCN)_n]^{2+}$ to form active oxygen complex $[(MeCN)_nCu^{II}\text{-}O\text{-}O\cdot]$, by which a highly efficient and mild cascade decarboxylation-oxyphosphorylation reaction is thus triggered. The prominent advantages of our reaction include using inexpensive $CuSO_4 \cdot 5H_2O$ as a catalyst, base or acid free and open air conditions as well as a wide reaction scope. The scope of the reaction encompasses alkenyl carboxylic acids, alkenes, as well as a series of organophosphorous reagents, including diphenylphosphine oxide, dialkyl *H*-phosphonates and ethyl phenylphosphinate. To our knowledge, it is the first example to show how active oxygen complex $[(MeCN)_nCu^{II}\text{-}O\text{-}O\cdot]$ is involved in the environmentally benign synthetic process of synthesizing a variety of biologically and chemically significant β-ketophosphonates. The investigation concerning using $[(MeCN)_nCu^{II}\text{-}O\text{-}O\cdot]$ as reaction initiator for other related synthetic approaches is currently underway.

4. Experimental Section

4.1. General information

All commercial reagents and solvents were used without further purification. ^1H, ^{13}C, and ^{31}P NMR spectra were recorded with a Bruker Avance 400 MHz spectrometer. All NMR spectra were recorded in $CDCl_3$ at room temperature (20 ± 3 °C). ^1H and ^{13}C chemical shifts are quoted in parts per million downfield from tetramethylsilane (TMS). ^{31}P chemical shifts are quoted in parts per million relative to 85% H_3PO_4 as an external standard. High resolution mass spectra (HR MS) were obtained with a Waters Micromass Q-Tof Micro instrument using the ESI technique.

4.2. General Procedure for the Synthesis of β-ketophosphonates

Starting from the alkenyl acids: alkenyl acids **1** (0.2 mmol), *H*-phosphonates **2** (0.4 mmol), and $CuSO_4 \cdot 5H_2O$ (10 mol%) were dissolved in 4 mL CH_3CN at round-bottomed flask and stirred at 60 °C for 6 h in an air atmosphere.

Starting from the alkenes: alkenes **4** (0.2 mmol), *H*-phosphonates **2** (0.3 mmol), and $CuSO_4 \cdot 5H_2O$ (10 mol%) were dissolved in 4 mL CH_3CN at round-bottomed flask and stirred at 60 °C for 3 h in an air atmosphere. Then, CH_3CN was evaporated, and the reaction mixture was quenched with water, followed by extraction with ethyl acetate. The combined organic layers were washed with brine and dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated in vacuo. The crude product was purified by silica gel chromatography (petroleum ether: ethyl acetate =1:1) to give the desired product.

4.3. Characterization data for products

Diethyl (2-oxo-2-phenylethyl)phosphonate (**3a**) [11]

Yellow oil, ^1H NMR ($CDCl_3$, 400 MHz,) δ: 7.89 (d, 2H, J = 7.6 Hz), 7.46 (t, 1H, J = 7.2 Hz), 7.35 (t, 2H, J = 7.6 Hz), 4.05-3.98 (m, 4H), 3.56 (d, 2H, J = 22.8 Hz), 1.15 (t, 6H, J = 7.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz); δ: 191.85 (d, $J_{P\text{-}C}$ = 6.5 Hz), 136.42 ($J_{P\text{-}C}$ = 1.9 Hz), 133.59, 128.92, 128.52, 62.59 (d, $J_{P\text{-}C}$ = 6.4 Hz), 38.78 (d, $J_{P\text{-}C}$ 129.3 Hz), 16.12 (d, $J_{P\text{-}C}$ = 6.4 Hz); ^{31}P NMR ($CDCl_3$, 162 MHz) δ: 17.76; HRMS: calcd for $C_{12}H_{17}O_4P$ $[M+H]^+$ 257.0937, found 257.0941.

Diisopropyl (2-oxo-2-phenylethyl)phosphonate (**3b**) [11]

Yellow oil, ^1H NMR ($CDCl_3$, 400 MHz,) δ: 7.98 (d, 2H, J = 7.2 Hz), 7.54 (t, 1H, J = 7.2 Hz), 7.39 (t, 2H, J = 8.0 Hz), 4.74-4.66 (m, 2H), 3.57 (d, 2H, J = 22.8 Hz), 1.24 (dd, 12H, J = 3.2 Hz, 6.4 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz); δ: 192.06 (d, $J_{P\text{-}C}$ = 6.6 Hz), 136.66, 133.48, 129.11, 128.47, 71.50 (d, $J_{P\text{-}C}$ = 6.6 Hz), 39.68 (d, $J_{P\text{-}C}$ = 129.6 Hz), 23.82 (dd, $J_{P\text{-}C}$ = 5.2 Hz, 21.3Hz); ^{31}P NMR ($CDCl_3$, 162 MHz) δ: 17.84; HRMS: calcd for $C_{14}H_{21}O_4P$ $[M+Na]^+$ 307.1070, found 307.1068

Diisobutyl (2-oxo-2-phenylethyl)phosphonate (**3c**)

Yellow oil, ^1H NMR ($CDCl_3$, 400 MHz,) δ: 7.91 (d, 2H, J = 7.2 Hz), 7.47 (t, 1H, J = 7.2 Hz), 7.36 (t, 2H, 8.0 Hz), 3.78-3.68 (m, 4H), 3.56 (d, 2H, J = 22.8 Hz), 1.83-1.73 (m, 2H), 0.77 (d, 6.8 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz); δ: 191.70 (d, $J_{P\text{-}C}$ = 6.9 Hz), 136.48 (d, $J_{P\text{-}C}$ = 1.4 Hz), 133.54, 128.96, 128.51, 72.31 (d, $J_{P\text{-}C}$ = 6.8 Hz), 38.04 (d, $J_{P\text{-}C}$ = 129.0 Hz), 29.03 (d, $J_{P\text{-}C}$ = 6.6 Hz), 18.50 (d, $J_{P\text{-}C}$ = 1.3 Hz); ^{31}P NMR ($CDCl_3$, 162 MHz) δ: 19.85; HRMS: calcd for $C_{16}H_{25}O_4P$ $[M+H]^+$ 313.1563, found 313.1572

Dibenzyl (2-oxo-2-phenylethyl)phosphonate (**3d**) [13c]

Yellow oil, ^1H NMR ($CDCl_3$, 400 MHz,) δ: 7.93 (d, 2H, J = 7.6 Hz), 7.54 (t, 1H, J = 7.2 Hz), 7.40 (t, 2H, J = 7.6 Hz), 7.34-7.28 (m, 10H), 5.09-4.98 (m, 4H), 3.68 (d, 2H, J = 22.4); ^{13}C NMR ($CDCl_3$, 100 MHz); δ: 191.71 (d, $J_{P\text{-}C}$ = 6.5 Hz), 136.44 (d, $J_{P\text{-}C}$ = 2.4 Hz), 135.90 (d, $J_{P\text{-}C}$ = 5.2 Hz), 133.72, 129.04, 128.66, 128.59, 128.51, 128.06, 68.08 (d, $J_{P\text{-}C}$ = 6.5 Hz), 38.68 (d, $J_{P\text{-}C}$ = 130.8); ^{31}P NMR ($CDCl_3$, 162 MHz) δ: 21.35; HRMS: calcd for $C_{22}H_{21}O_4P$ $[M+H]^+$ 381.1250, found 381.1256

Diphenyl (2-oxo-2-phenylethyl)phosphonate (**3e**)[6a]

Yellow oil, ^1H NMR ($CDCl_3$, 400 MHz,) δ: 8.04 (d, 2H, J = 7.2 Hz), 7.61 (t, 1H, J = 7.2 Hz), 7.50 (t, 2H, 7.6 Hz), 7.32-7.18 (m, 4H), 7.17-7.15 (m, 6H), 3.94 (d, 2H, 22.8 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz); δ: 190.78 (d, $J_{P\text{-}C}$ = 6.9 Hz), 150.03 (d, $J_{P\text{-}C}$ = 8.9 Hz), 136.42, 133.97, 129.82, 129.08, 128.79, 125.49, 120.60 (d, $J_{P\text{-}C}$ = 4.4 Hz), 37.86 (d, 132.7 Hz); ^{31}P NMR ($CDCl_3$, 162 MHz) δ: 13.14; HRMS: calcd for $C_{20}H_{17}O_4P$ $[M+H]^+$ 353.0937, found 353.0941

2-(diphenylphosphoryl)-1-phenylethan-1-one (**3f**) [13c]

White solid, ^1H NMR ($CDCl_3$, 400 MHz,) δ: 7.95 (d, 2H, J = 7.6 Hz), 7.81-7.76(m, 4H), 7.49-7.35 (m, 9H), 4.13 (d, 2H, J = 15.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz); δ: 192.86 (d, $J_{P\text{-}C}$ =5.6 Hz), 136.95, 133.61, 132.27 (d, $J_{P\text{-}C}$ = 5.2 Hz), 132.18, 131.20 (d, $J_{P\text{-}C}$ = 4.8 Hz), 129.23, 128.70, 128.55 (d, $J_{P\text{-}C}$ = 4.5 Hz), 43.13 (d, $J_{P\text{-}C}$ = 58.0 Hz); ^{31}P NMR ($CDCl_3$, 162 MHz) δ: 26.96; HRMS: calcd for $C_{20}H_{17}O_2P$ $[M+H]^+$ 321.1039, found 321.1040.

Ethyl (2-oxo-2-phenylethyl)(phenyl)phosphonate (**3g**) [11]

Yellow oil, ^{1}H NMR ($CDCl_3$, 400 MHz,) δ: 7.94 (dd, 2H, J = 0.8, 8.0 Hz), 7.79-7.73 (m, 2H), 7.55-7.50 (m, 2H), 7.45-7.39 (m, 4H), 4.15-3.87 (m, 2H), 3.78 (dd, 2H, J_{P-H} = 4.8Hz, 18.8Hz), 1.23 (t, 3H, J = 6.8 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz); δ: 192.12 (d, J_{P-C} = 5.5 Hz), 136.86, 133.54, 132.73 (d, J_{P-C} = 2.8 Hz), 131.87 (d, J_{P-C} = 10.2 Hz), 130.65 (d, J_{P-C} = 132.0 Hz), 129.49, 128.90 (d, J_{P-C} = 13.2 Hz) 128.56, 61.50 (d, J_{P-C} = 6.3 Hz), 43.05 (d, J_{P-C} = 85.8 Hz), 16.33 (d, J_{P-C} = 6.5 Hz); ^{31}P NMR ($CDCl_3$, 162 MHz) δ: 33.69; HRMS: calcd for $C_{16}H_{17}O_3P$ $[M+Na]^+$ 311.0808, found 311.0810

Diethyl (2-oxo-2-(p-tolyl)ethyl)phosphonate (**3h**) [13c]

yellow oil, ^{1}H NMR ($CDCl_3$, 400 MHz,) δ: 7.90 (d, 2H, J = 8.0 Hz), 6.25 (d, 2H, J = 8.0 Hz), 4.16-4.09 (m, 4H), 3.60 (d, 2H, 22.8 Hz), 2.40 (3H), 1.27 (t, 6H, J = 7.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz); δ: 191.47 (d, J_{P-C} = 6.5 Hz), 144.68, 134.08, 129.30, 129.25, 62.68 (d, J_{P-C} = 6.5 Hz), 38.48 (d, J_{P-C} = 129.4 Hz), 21.69, 16.24 (d, J_{P-C} = 6.2 Hz); ^{31}P NMR ($CDCl_3$, 162 MHz) δ: 21.25; HRMS: calcd for $C_{13}H_{19}O_4P$ $[M+H]^+$ 271.1094, found 271.1096.

Diisopropyl (2-oxo-2-(p-tolyl)ethyl)phosphonate (**3i**) [11]

Yellow oil, ^{1}H NMR ($CDCl_3$, 400 MHz,) δ: 7.90 (d, 2H, J =8.0 Hz), 7.24 (d, 2H, J = 7.6 Hz), 4.77-4.66 (m, 6H), 3.57 (d, 2H, J = 22.8 Hz), 2.39 (3H), 1.27 (dd, 12H, J = 4.0 Hz, 6.4Hz); ^{13}C NMR ($CDCl_3$, 100 MHz); δ: 191.61 (d, J_{P-C} = 6.6 Hz), 144.46, 134.22, 129.29, 129.19, 71.61 (d, J_{P-C} = 6.7 Hz), 39.62 (d, J_{P-C} = 130.0 Hz), 23.84 (dd, J_{P-C} = 5.2 Hz, 21.7 Hz), 21.67; ^{31}P NMR ($CDCl_3$, 162 MHz) δ: 22.84; HRMS: calcd for $C_{15}H_{23}O_4P$ $[M+Na]^+$ 321.1226, found 321.1228.

Dibenzyl (2-oxo-2-(p-tolyl)ethyl)phosphonate (**3j**)

Yellow oil, ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.83 (d, 2H, J = 7.6 Hz), 7.27 (10H), 7.28 (d, 2H, J = 7.6 Hz), 5.08-4.97 (m, 4H), 3.61 (d, 2H, J = 22.4 Hz), 2.36 (3H); ^{13}C NMR ($CDCl_3$, 100 MHz); δ: 191.27 (d, J_{P-C} = 6.4), 144.66, 135.98 (d, J_{P-C} = 6.2 Hz), 134.03 (d, J_{P-C} = 2.5 Hz), 129.34, 129.20, 128.56, 128.45, 128.04, 67.97 (d, 6.2 Hz), 38.65 (d, J_{P-C} = 130.5Hz), 21.71; ^{31}P NMR ($CDCl_3$, 162 MHz) δ: 21.52; HRMS: calcd for $C_{23}H_{23}O_4P$ $[M+H]^+$ 395.1407, found395.1412

2-(diphenylphosphoryl)-1-(p-tolyl)ethan-1-one (**3k**) [12]

White solid, ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.82-7.78 (m, 6H), 7.42 (t, 2H, J = 7.2 Hz), 7.34-7.29 (m, 4H), 7.09 (d, 2H, J = 8.0 Hz), 4.30 (d, 2H, J = 15.2 Hz), 2.29 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz); δ: 193.36, 144.76, 134.43, 132.24 (d, J_{P-C} = 2.2 Hz), 131.24 (d, J_{P-C} = 10.4 Hz), 131.54, 131.44, 129.52, 129.33, 128.64 (d, J_{P-C} = 12.4 Hz), 42.59 (d, J_{P-C} = 60.1 Hz), 21.75; ^{31}P NMR ($CDCl_3$, 162 MHz) δ: 28.35; HRMS: calcd for $C_{21}H_{19}O_2P$ $[M+H]^+$ 335.1195, found 335.1198.

Diethyl (2-oxo-2-(o-tolyl)ethyl)phosphonate (**3l**) [13c]

Yellow oil, ^{1}H NMR ($CDCl_3$, 400 MHz,) δ: 7.75 (d, 1H, J = 8.0 Hz , 7.39 (t, 1H, J = 6.2 Hz), 7.31-7.25 (m, 2H), 4.16-4.08 (m, 4H), 3.60 (d, 2H, J = 22.4 Hz), 2.52 (3H), 1.27 (t, 6H, J = 5.8 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz); δ: 195.03 (d, J_{P-C} = 6.5 Hz), 138.96, 137.21, 131.96 (d, J_{P-C} = 4.2 Hz), 129.60, 125.69, 62.59 (d, J_{P-C} = 6.4 Hz), 41.00 (d, J_{P-C} =126.9 Hz), 21.30, 16.19 (d, J_{P-C} = 6.2 Hz); ^{31}P NMR ($CDCl_3$, 162 MHz) δ: 20.32; HRMS: calcd for $C_{13}H_{19}O_4P$ $[M+H]^+$ 271.1094, found 271.1097.

Diisopropyl (2-oxo-2-(o-tolyl)ethyl)phosphonate (**3m**) [11]

Yellow oil, ^{1}H NMR ($CDCl_3$, 400 MHz,) δ: 7.72 (d, 1H, J = 7.6 Hz), 7.37 (t, 1H, J = 7.2 Hz), 7.28-7.22 (m, 2H), 4.75-4.67 (m, 2H), 3.56 (d, 2H, J = 22.8 Hz), 2.50 (3H), 1.25 (dd, 12H, J = 6.4 Hz, 8.4 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz); δ: 195.34 (d, J_{P-C} = 6.7 Hz), 138.77, 137.56, 131.77 (d, J_{P-C} = 5.3 Hz), 129.62, 125.57, 71.45 (d, J_{P-C} = 6.6 Hz), 42.89 (d, J_{P-C} =129.2 Hz), 29.70, 23.82 (dd, J_{P-C} = 3.8 Hz, 21.2 Hz), 21.23; ^{31}P NMR ($CDCl_3$, 162 MHz) δ: 18.25; HRMS: calcd for $C_{15}H_{23}O_4P$ $[M+H]^+$ 299.1407, found 299.1401.

Diisobutyl (2-oxo-2-(o-tolyl)ethyl)phosphonate (**3n**)

Yellow oil, ^{1}H NMR ($CDCl_3$, 400 MHz,) δ: 7.72 (d, 1H, J = 7.6 Hz), 7.35 (t, 1H, J = 6.8 Hz), 7.26-7.20 (m, 2H), 3.78 (t, 4H, J = 6.8 Hz), 3.59 (d, 2H, J = 22.8 Hz), 2.48 (3H), 1.86-1.80 (m, 2H), 0.84 (d, 12H, J = 6.4 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz); δ: 194.90 (d, J_{P-C} = 6.7 Hz), 138.99, 137.20, 131.95 (d, J_{P-C} = 8.0 Hz), 129.65, 125.69, 72.33 (d, J_{P-C} = 6.7 Hz), 41.26 (d, J_{P-C} =128.4 Hz), 29.10 (d, J_{P-C} = 6.6 Hz), 21.33, 18.58 (d, J_{P-C} = 1.2 Hz); ^{31}P NMR ($CDCl_3$, 162 MHz) δ: 18.51; HRMS: calcd for $C_{17}H_{27}O_4P$ $[M+H]^+$ 327.1720, found 327.1724.

Diethyl (2-(4-methoxyphenyl)-2-oxoethyl)phosphonate (**3o**) [10b]

Yellow oil, ^{1}H NMR ($CDCl_3$, 400 MHz,) δ: 7.97 (d, 2H, J = 8.8 Hz), 6.92 (d, 2H, J = 8.8 Hz), 4.16-4.08 (m, 4H), 3.85 (s, 3H), 3.58 (d, 2H, J = 22.8 Hz), 1.27 (t, 6H, J = 7.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz); δ: 190.23 (d, J_{P-C} = 6.1 Hz), 164.02, 131.51, 129. 60 (d, J_{P-C} = 2.0 Hz), 113.78, 62.70 (d, J_{P-C} = 7.5Hz), 55.52, 38.20 (d, J_{P-C} = 129.3Hz), 16.24 (d, J_{P-C} = 6.3 Hz); ^{31}P NMR ($CDCl_3$, 162 MHz) δ: 20.70; HRMS: calcd for $C_{13}H_{19}O_5P$ $[M+Na]^+$ 309.0862, found 309.0861.

Diisobutyl (2-(4-methoxyphenyl)-2-oxoethyl)phosphonate (**3p**)

Yellow oil, ^{1}H NMR ($CDCl_3$, 400 MHz,) δ: 7.96 (d, 2H, J = 8.8 Hz), 6.89 (d, 2H, J = 8.8 Hz), 3.83 (s, 3H), 3.82-3.72 (m, 4H), 3.56 (d, 2H, J = 22.8 Hz), 1.90-1.80 (m, 2H), 0.84 (d, 12H, J = 6.8 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz); δ: 190.13 (d, J_{P-C} = 6.6 Hz), 163.95, 131.49, 129.63, 113.74, 72.37 (d, J_{P-C} = 7.8 Hz), 55.49, 37.76 (d, J_{P-C} = 129.0 Hz), 29.13 (d, J_{P-C} = 6.5 Hz), 18.58 (d, J_{P-C} = 1.1 Hz); ^{31}P NMR ($CDCl_3$, 162 MHz) δ: 20.6; HRMS: calcd for $C_{17}H_{27}O_5P$ $[M+H]^+$ 343.1669, found 343.1674.

Diethyl (2-(4-fluorophenyl)-2-oxoethyl)phosphonate (**3q**) [10b]

Yellow oil, ^{1}H NMR ($CDCl_3$, 400 MHz,) δ: 8.03-8.00 (dd, 2H, J = 5.6 Hz, 8.8 Hz), 7.10 (t, 2H, J = 8.4 Hz), 4.12-4.05 (m, 4H), 3.56 (d, 2H, J = 22.8 Hz), 1.24(t, 6H, J = 7.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz); δ: 190.28 (d, J_{P-C} = 6.5 Hz), 166.15 (d, J_{F-C} = 254.5 Hz), 132.93, 131.80 (d, J_{F-C} = 9.4 Hz), 115.75 (d, J_{F-C} = 21.8 Hz), 62.75 (d, J_{P-C} = 6.5 Hz), 38.64 (d, J_{P-C} = 128.8 Hz), 16.19 (d, J_{P-C} = 6.3 Hz); ^{31}P NMR ($CDCl_3$, 162 MHz) δ: 19.69; HRMS: calcd for $C_{12}H_{16}FO_4P$ $[M+H]^+$ 275.0843, found 275.0846.

Diisopropyl (2-(4-fluorophenyl)-2-oxoethyl) phosphonate (**3r**) [11]

Yellow oil, ^{1}H NMR ($CDCl_3$, 400 MHz,) δ: 8.04 (dd, 2H, J = 5.6 Hz, 8.4 Hz), 7.12 (t, 2H, J = 8.8 Hz), 4.76-4.65 (m, 2H), 3.55 (d, 2H, 5-H, J = 23.2 Hz), 1.26 (dd, 12H, J = 1.2 Hz, 6.0 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz); δ: 190.44 (d, J_{P-C} = 6.5 Hz), 166.01 (d, J_{F-C} = 254.3 Hz), 133.10, 131.92 (d, J_{F-C} = 9.5 Hz), 115.60 (d, J_{F-C} = 21.8 Hz), 71.65 (d, J_{P-C} = 6.7 Hz), 39.78 (d, J_{P-C} = 129.1 Hz), 23.83 (dd, J_{P-C} = 3.8 Hz, 17.6 Hz); ^{31}P NMR ($CDCl_3$, 162 MHz) δ: 17.41; HRMS: calcd for $C_{14}H_{20}FO_4P$ $[M+Na]^+$ 325.0975, found 325.0979.

Diisobutyl (2-(4-fluorophenyl)-2-oxoethyl)phosphonate (**3s**)

Yellow oil, ^{1}H NMR ($CDCl_3$, 400 MHz,) δ: 8.00 (dd, 2H, J = 5.2 Hz, 8.8 Hz), 7.08 (t, 2H, J = 8.8 Hz), 3.82-3.73 (m, 4H), 3.56 (d, 2H, J = 23.2 Hz), 1.87-1.77 (m, 2H), 0.82 (d, 12H, J = 6.8 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz); δ: 190.16 (d, J_{P-C} = 6.6 Hz), 165.52 (d, J_{F-C} = 254.4 Hz), 132.94, 131.80 (d, J_{F-C} = 9.4 Hz), 115.68 (d, J_{F-C} = 21.8 Hz), 72.42 (d, J_{P-C} = 9.6 Hz), 38.17 (d, J_{P-C} = 128.6 Hz), 29.08 (d, J_{P-C} = 6.5 Hz), 18.51; ^{31}P NMR ($CDCl_3$, 162 MHz) δ: 18.64; HRMS: calcd for $C_{16}H_{24}O_4P$ $[M+H]^+$ 331.1469, found 331.1475.

Diethyl (2-(4-bromophenyl)-2-oxoethyl)phosphonate (**3t**)[10b]

Yellow oil, ^{1}H NMR ($CDCl_3$, 400 MHz,) δ: 7.86 (d, 2H, J = 8.4 Hz), 7.59 (d, 2H, J = 7.6 Hz), 4.15-4.08 (m, 4H), 3.58 (d, 2H, J = 22.8 Hz), 1.27 (t, 6H, J = 8.8 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz); δ: 190.92 (d, J_{P-C} = 6.5 Hz), 135.20, 131.93, 130.58, 129.10 (d, J_{P-C} = 4.5 Hz), 62.81 (d, J_{P-C} = 6.5 Hz), 38.21 (d, J_{P-C} = 128.6 Hz), 16.24 (d, J_{P-C} = 6.3 Hz); ^{31}P NMR ($CDCl_3$, 162 MHz) δ: 19.30; HRMS: calcd for $C_{12}H_{16}BrO_4P$ $[M+H]^+$ 335.0042, found 335.0041.

Diisopropyl (2-(4-bromophenyl)-2-oxoethyl)phosphonate (**3u**)[11]

Yellow oil, ^{1}H NMR ($CDCl_3$, 400 MHz,) δ: 7.82 (d, 2H, J = 8.4Hz), 7.54 (d, 2H, J = 8.8 Hz), 4.69-4.61 (m, 2H), 3.49 (d, 2H, J = 23.3 Hz), 1.20 (dd, 12H, J = 2.4 Hz, 6.0 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz); δ: 191.16 (d, J_{P-C} = 6.6 Hz), 135.42, 131.88, 130.78, 128.93, 71.67 (d, J_{P-C} = 6.7 Hz), 39.96 (d, J_{P-C} = 128.7 Hz), 23.96 (dd, J_{P-C} = 5.2 Hz, 18.9 Hz); ^{31}P NMR ($CDCl_3$, 162 MHz) δ: 16.97; HRMS: calcd for $C_{14}H_{20}BrO_4P$ $[M+Na]^+$ 385.0175, found 385.0175.

Diisobutyl (2-(4-bromophenyl)-2-oxoethyl)phosphonate (**3v**)

Yellow oil, ^{1}H NMR ($CDCl_3$, 400 MHz,) δ: 7.77 (d, 2H, J = *7.2* Hz), 7.48 (d, 2H, J = 8.4 Hz), 3.75-3.67 (m, 4H), 3.50 (d, 2H, J = 22.8 Hz), 1.81-1.71 (m, 2H), 0.76 (d, 12H, J = 6.8 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz); δ: 190.71 (d, J_{P-C} = 6.7 Hz), 135.17, 131.80, 130.52, 128.85, 72.34 (d, J_{P-C} = 7.1 Hz), 38.20 (d, J_{P-C} = 128.2 Hz), 29.03 (d, J_{P-C} = 6.6 Hz), 18.51; ^{31}P NMR ($CDCl_3$, 162 MHz) δ: 19.25; HRMS: calcd for $C_{16}H_{24}O_4BrP$ $[M+H]^+$ 391.0668, found 391.0672.

Diethyl (2-(4-nitrophenyl)-2-oxoethyl)phosphonate (**3w**)[18]

Yellow oil, ^{1}H NMR ($CDCl_3$, 400 MHz,) δ: 8.31 (d, 2H, J = 8.8 Hz), 8.18 (d, 2H, J = 8.8 Hz), 4.18-4.11 (m, 4H), 3.67 (d, 2H, J = 23.2 Hz), 1.28 (t, 6H, J = 7.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz); δ: 190.63 (d, J_{P-C} = 6.7 Hz), 150.57, 140.77, 130.15, 123.79, 63.09 (d, J_{P-C} = 6.5 Hz), 39.27 (d, J_{P-C} = 128.0 Hz), 16.24 (d, J_{P-C} = 6.3 Hz); ^{31}P NMR ($CDCl_3$, 162 MHz) δ: 18.70; HRMS: calcd for $C_{12}H_{16}NO_6P$ $[M+H]^+$ 302.0788, found 302.0791.

Diisopropyl (2-(4-nitrophenyl)-2-oxoethyl)phosphonate (**3x**)

Yellow oil, ^{1}H NMR ($CDCl_3$, 400 MHz,) δ: 8.29 (d, 2H, J = 8.8 Hz), 8.18 (d, 2H, J = 8.4 Hz), 4.75-4.67 (m, 2H), 3. 61 (d, 2H, J = 22.8 Hz), 1.26 (d, 12H, 6.0 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz); δ: 190.72 (d, J_{P-C} = 6.9 Hz), 150.46, 140.95, 130.21, 123.68, 71.93 (d, J_{P-C} = 6.8 Hz), 40.04 (d, J_{P-C} = 128.0 Hz), 23.90 (dd, J_{P-C} = 3.9 Hz, 13.9 Hz); ^{31}P NMR ($CDCl_3$, 162 MHz) δ: 16.44; HRMS: calcd for $C_{14}H_{20}NO_6P$ $[M+H]^+$ 330.1101, found 330.1104.

Diisobutyl (2-(4-nitrophenyl)-2-oxoethyl)phosphonate (**3y**)

Yellow oil, ^{1}H NMR ($CDCl_3$, 400 MHz,) δ: 8.31 (d, 2H, J = 8.8 Hz), 8.19 (d, 2H, J = 8.8 Hz), 3.88-3.79 (m, 4H), 3.68 (d, 2H, J = 23.2 Hz), 1.93-18.3 (m, 2H), 0.87 (d, 12H, J = 6.8 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz); δ: 194.89 (d, J_{P-C} = 6.6 Hz), 138.98, 137.21, 129.64, 125.69, 72.37 (d, J_{P-C} = 7.0 Hz), 40.76 (d, J_{P-C} = 128.4 Hz), 29.10 (d, J_{P-C} = 6.6 Hz), 18.58; ^{31}P NMR ($CDCl_3$, 162 MHz) δ: 20.35; HRMS: calcd for $C_{16}H_{24}NO_6P$ $[M+H]^+$ 358.1414, found 358.1418.

Diethyl (2-(furan-2-yl)-2-oxoethyl)phosphonate (**3z**)[13c]

Yellow oil, ^{1}H NMR ($CDCl_3$, 400 MHz,) δ: 7.56 (s, 1H), 7.23 (d, 1H, J = 3.2 Hz), 6.50 (q, 1H, J = 1.2 Hz, 3.6 Hz), 4.10-4.03 (m, 4H), 3.42 (d, 2H, J = 22.4 Hz), 1.21 (t, 6H, J = 6.8 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz); δ: 179.92 (d, J_{P-C} = 6.9 Hz), 152.20, 147.16, 118.96, 112.74, 62.63 (d, J_{P-C} = 6.4 Hz), 38.10 (d, J_{P-C} = 129.1 Hz), 16.18 (d, J_{P-C} = 6.3 Hz); ^{31}P NMR ($CDCl_3$, 162 MHz) δ: 19.50; HRMS: calcd for $C_{10}H_{15}O_5P$ $[M+H]^+$ 247.0730, found 247.0736.

Diisobutyl (2-(furan-2-yl)-2-oxoethyl)phosphonate (**3aa**)

Yellow oil, ^{1}H NMR ($CDCl_3$, 400 MHz,) δ: 7.60 (d, 1H, J = 0.8 Hz), 7.27 (d, 1H, J = 8.4 Hz), 6.54 (d, 1H, J = 1.6 Hz, 3.6 Hz), 3.87-3.77 (m, 4H), 3.49 (d, 2H, J = 22.8 Hz), 1.92-1.82 (m, 2H), 0.86 (d, 12H, J = 6.8 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz); δ: 179.95 (d, J_{P-C} = 7.0 Hz), 152.33, 147.06, 118.81, 112.86, 72.41 (d, J_{P-C} = 7.0 Hz), 37.89 (d, J_{P-C} = 129.2 Hz), 29.11 (d, J_{P-C} = 6.6 Hz), 18.56; ^{31}P NMR ($CDCl_3$, 162 MHz) δ: 18.38; HRMS: calcd for $C_{14}H_{23}O_5P$ $[M+H]^+$ 303.1356, found 303.1360.

Diethyl (1-oxo-1-phenylpropan-2-yl)phosphonate (**3ab**)[12]

Yellow oil, ^{1}H NMR ($CDCl_3$, 400 MHz,) δ: 7.99 (d, 2H, J = 7.2 Hz), 7.57 (t, 1H, J = 7.6 Hz), 7.47 (t, 2H, J = 7.6 Hz), 4.16-4.03 (m, 5H), 1.54 (dd, 3H, J = 5.6 Hz, 18.0 Hz), 1.28 (t, 6H, J = 7.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz); δ: 196.70 (d, J_{P-C} = 5.0 Hz), 137.07, 133.54, 129.06, 128.70, 62.90 (dd, J = 6.8 Hz, J_{P-C} = 10.3 Hz), 41.50 (d, J_{P-C} = 129.5 Hz), 16.47 (dd, J_{P-C} = 6.0 Hz, 14.5 Hz), 12.43 (d, J_{P-C} = 6.6 Hz); ^{31}P NMR ($CDCl_3$, 162 MHz) δ: 22.31; HRMS: calcd for $C_{13}H_{19}O_4P$ $[M+H]^+$ 271.1094, found 271.1094.

Diethyl (2-(4-(tert-butyl)phenyl)-2-oxoethyl)phosphonate (**3ac**)[13c]

Yellow oil, ^{1}H NMR ($CDCl_3$, 400 MHz,) δ: 7.87 (d, 2H, J = 8.4 Hz), 7.40 (d, 2H, J = 8.8 Hz), 4.08-4.01 (m, 4H), 3.53 (d, 2H, J = 22.8 Hz), 1.25 (s, 9H), 1.92 (t, 6H, J = 7.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz); δ: 191.41 (d, J_{P-C} = 6.5 Hz), 157.39, 133.93 (d, J_{P-C} = 1.9 Hz), 129.00, 125.50, 62.53 (d, J_{P-C} = 6.5 Hz), 38.30 (d, J_{P-C} = 129.1 Hz), 35.09, 30.97, 16.18 (d, J_{P-C} = 6.3 Hz); ^{31}P NMR ($CDCl_3$, 162 MHz) δ: 19.77; HRMS: calcd for $C_{16}H_{25}O_4P$ $[M+H]^+$ 313.1563, found 313.1569.

Diisobutyl (2-(4-(tert-butyl)phenyl)-2-oxoethyl)phosphonate (**3ad**)

Yellow oil, ^{1}H NMR ($CDCl_3$, 400 MHz,) δ: 7.89 (d, 2H, J = 8.8 Hz), 7.42 (d, 2H, J = 8.4 Hz), 3.82-3.73 (m, 4H), 3.57 (d, 2H, J = 22.8 Hz), 1.87-1.77 (m, 2H), 1.28 (s, 9H), 0.81 (d, J = 6.8 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz); δ: 191.37 (d, J_{P-C} = 6.5 Hz), 157.37, 134.02, 129.03, 125.51, 72.30 (d, J_{P-C} = 6.8 Hz), 37.95 (d, J_{P-C} = 6.8 Hz), 35.10, 31.00, 29.07 (d, J_{P-C} = 6.6 Hz), 18.55 (d, J_{P-C} = 2.0 Hz); ^{31}P NMR ($CDCl_3$, 162 MHz) δ: 19.85; HRMS: calcd for $C_{20}H_{33}O_4P$ $[M+H]^+$ 369.2189, found 369.2194.

Diethyl (2-oxo-3-phenoxypropyl)phosphonate (**3ae**)[12]

Yellow oil, ^{1}H NMR ($CDCl_3$, 400 MHz,) δ: 7.31-7.27 (dd, 2H, J = 0.8 Hz, 8.7 Hz), 7.00 (t, 1H, J = 7.2 Hz), 6.94 (dd, 2H, J = 0.8 Hz, J = 8.7 Hz), 4.71 (s, 2H), 4.20-4.12(m, 4H), 3.27 (d, 2H, J = 22.8 Hz), 1.32 (t, 6H, J = 6.8 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz); δ: 198.87 (d, J_{P-C} = 6.6 Hz), 157.69, 129.86, 122.03, 114.75, 72.86, 63.03 (d, J_{P-C} = 6.3 Hz), 38.70 (d, J_{P-C} = 127.0 Hz), 16.47 (d, J_{P-C} = 6.3 Hz); ^{31}P NMR ($CDCl_3$, 162 MHz) δ: 18.43; HRMS: calcd for $C_{15}H_{23}O_5P$ $[M+H]^+$ 287.1043, found 287.1043.

Diethyl (1-oxo-2,3-dihydro-1H-inden-2-yl)phosphonate (**3af**)

Yellow oil, ^{1}H NMR ($CDCl_3$, 400 MHz,) δ: 7.74 (d, 1H, J = 7.6 Hz), 7.58 (t, 1H, J = 7.2 Hz), 7.46 (d, 1H, J = 7.6 Hz), 7.36 (t, 1H, J = 7.6 Hz), 4.19-4.08 (m, 4H), 3.54-3.35 (m, 2H), 3.32-3.23 (m, 1H), 1.31 (t, 3H, J = 6.8 Hz), 1.21 (t, 3H, J = 7.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz); δ: 199.17 (d, J_{P-C} = 4.8 Hz), 153.13 (d, J_{P-C} = 5.4 Hz), 136.43 (d, J_{P-C} = 3.6 Hz), 135.07, 127.70, 126.41, 124.33, 63.00 (dd, J_{P-C} = 6.7 Hz, 48.4 Hz), 46.03 (d, J_{P-C} = 136.4 Hz), 28.61 (d, J_{P-C} = 2.8 Hz), 16.30 (t, J_{P-C} = 5.0 Hz); ^{31}P NMR ($CDCl_3$, 162 MHz) δ: 22.68; HRMS: calcd for $C_{13}H_{17}O_4P$ $[M+H]^+$ 269.0937, found 269.0940.

Diethyl (1-(4-methoxyphenyl)-1-oxopropan-2-yl)phosphonate (**3ag**)

Yellow oil, ^{1}H NMR ($CDCl_3$, 400 MHz,) δ: 7.91 (d, 2H, J = 8.8 Hz), 6.86 (d, 2H, J = 8.8 Hz), 4.08-3.95 (m, 5H), 3.78 (s, 3H),

1.46-1.40 (dd, 3H, J = 6.8 Hz, 18.0 Hz), 1.20 (t, 3H, J = 7.2 Hz), 1.13 (t, 3H, J = 7.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz); δ: 194.64 (d, J_{P-C} = 4.8 Hz), 163.73, 131.22, 129.63, 113.59, 62.55 (dd, J_{P-C} = 2.3 Hz, 6.7 Hz), 55.44, 40.71 (d, J_{P-C} = 129.6 Hz), 16.26 (dd, J_{P-C} = 6.0 Hz, 18.9 Hz), 12.25 (d, J_{P-C} = 5.4 Hz); ^{31}P NMR ($CDCl_3$, 162 MHz) δ: 23.93; HRMS: calcd for $C_{14}H_{21}O_5P$ $[M+H]^+$ 301.1199, found 301.1203.

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Supplementary Material

Copies of ^{1}H NMR, ^{13}C NMR, and ^{31}P NMR of products.

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