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ARTICLE

An Easy Access to α-Aryl Substituted γ-Ketophosphonates: Lewis Acid Mediated Reactions of 1,3-diketones with α-hydroxyphosphonates and Tandem Regioselective C-C Bond Cleavage

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A range of α-aryl substituted γ-ketophosphonates is synthesised by Lewis acid mediated reactions of 1,3-diketones and easily accessible, inexpensive benzylic α-hydroxyphosphonates in an operationally-simple method under solvent-free conditions without exclusion of air/moisture. A regioselective C-C bond cleavage for 1,3-diketones in a tandem fashion has also been demonstrated. Synthesis of a γ-ketophosphonate with phenol functionality at α- position (structural analogue of raspberry ketone, a natural product) has also been presented.

Introduction

Among organophosphonates, γ-ketophosphonates have received significant concern in synthetic and biological chemistry as they exhibit an extensive range of biological activities such as herbicides, fungicides and several enzyme [matrix-metalloprotease (MMP-2), kininogenase, osteoclastic acid phosphatase (OAP)] inhibitors.[1-3] Notably, the presence of a substituent at α-position plays a key role to make these γ-ketophosphonates (such as **A-C**; Fig 1) more biologically active.[1-2] Furthermore, these γ-ketophosphonates have also been considered as precursors for the synthesis of γ-hydroxyphosphonates[3b] and also to synthesise *methylenomycin-B*, a natural product that belongs to a family of cyclopentanoid antibiotics.[3a] Thus, the synthesis of new α-aryl-substituted γ-keto phosphonates is highly desirable.

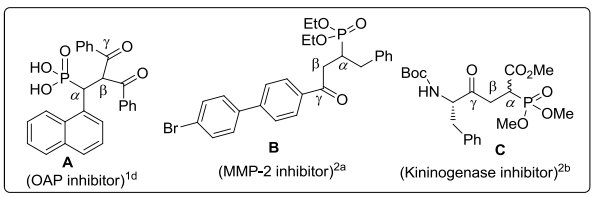
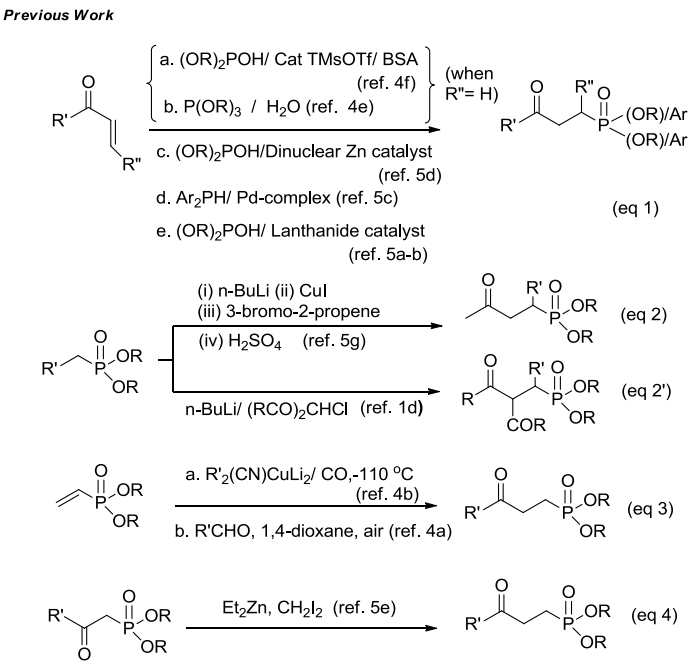


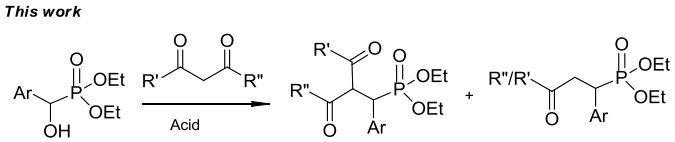
Fig. 1 Examples of biologically significant *α-substituted* γ-ketophosphonates.

Some methods available for the synthesis of *α- substituted* and *unsubstituted* γ-ketophosphonates are presented in eq 1-4.[4-5] The conjugate addition of phosphites/phosphines with enones is the most common approach (routes a-e, eq 1). Using the same starting materials, γ-ketophosphonates were synthesised in both optically active/inactive forms in the presence of palladium[5c] or organozinc[5d] compounds (route c or d, eq 1). Recently, some research groups have accomplished the synthesis of these compounds by the treatment of *α,β*-unsaturated carbonyl compounds with phosphites/phosphines in the presence of expensive lanthanide complexes (route e, eq 1).[5a-b] The traditional route *via* deprotonation of alkylphosphonate using the strong, air/moisture sensitive base *n*-BuLi followed by the treatment of toxic halogenated compounds is also well known (eq 2 & 2'). Reported aerobic hydroacylation of vinylphosphonates (eq 3) was ineffective to afford *α- substituted* γ-ketophosphonates.[4a]



The $ZnEt_2/CH_2I_2$ mediated chain extension reaction starting from *β*-ketophosphonates has also been described (eq 4).[5e] It is worth noting that organozinc compounds should be handled with enough care as these are highly pyrophoric and quite expensive compared to other common Lewis acids such as Fe(III), Bi(III) etc.

In our continuing efforts on acid mediated synthesis of *α-substituted* organophosphonates,[6] we presently report a handy and economical Lewis acid mediated route to access a range of *α*-aryl substituted γ-ketophosphonates from easily accessible *α*-hydroxyphosphonates and 1,3-diketones mostly under solvent–free conditions (eq 5).



(eq 5)

Even though Lewis acid catalysed benzylation of 1,3-diketones is familiar,[7] the presence of phosphoryl group makes the chemistry more interesting[3c-e] to afford the biologically important γ-ketophosphonates efficiently in a convenient protocol. A subsequent regioselective C-C bond cleavage for the phosphoryl substituted 1,3-diketones is observed via tandem fashion on employing different reaction conditions *exclusive of any separate alcohol treatment.* The iron(III)/other metal mediated C-C bond cleavage to produce a ketone is known in the literature only *in the presence of alcohol*.[8]

Results and discussion

In our present study *α*-hydroxyphosphonates (**1a-e,** Fig. 2, synthesised by following Pudovik reactions of phosphite and aldehydes)[9] and 1,3-diketones (**2a-d**, Fig 2) were preferred with a consideration of accessibility, structural reactivity and diversity.

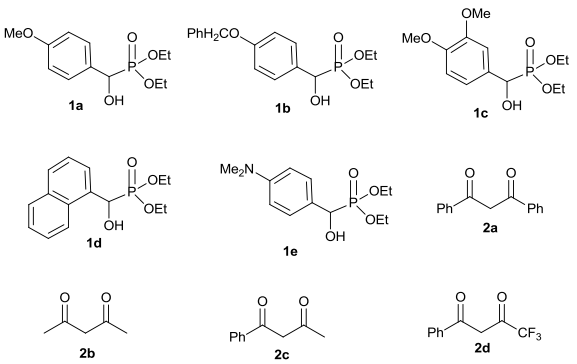
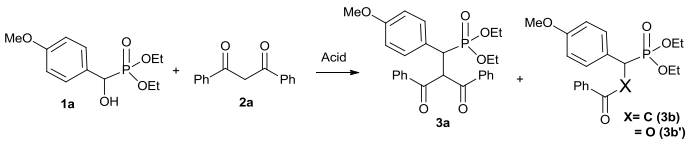


Fig. 2 The phosphonates and 1,3-diketones used as precursors

The initial study was focused on the screening of different acids for the reactions of easily accessible inexpensive phosphonate (**1a)** and symmetrical 1,3-diketone (**2a)** to afford the γ-ketophosphonates **3a** and **3b** where **3b** is a C-C bond cleaved product. It was found that the acids, solvent and temperature affect the product ratio (**3a**:**3b**) significantly (Table 1). Brønsted acids such as triflic acid (TfOH) and *p*-toluenesulfonic acid (p-TSA) were also quite effective[10] (entries 14-16, Table 1) for this reaction but are not much explored herein.

Table 1 Reactions of **1a** with **2a** under different reaction conditions[a]



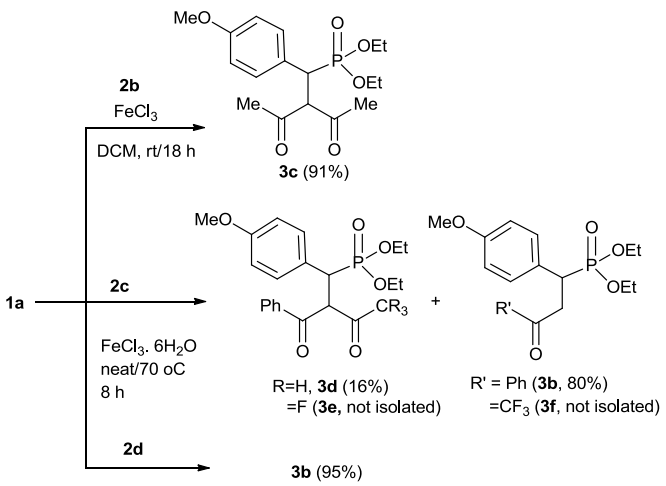
Entry	Acid	Solvent	Time(h)/Temp (°C)	Isolated yield:**3a/3b**
1.	$FeCl_3$	neat	8/70	90/trace
2.	$FeCl_3$	nitromethane	10/70	90/trace
3	$FeCl_3$	nitromethane	6/28	90/0
4	$FeCl_3$	dichloroethane	8/28	85/0
5.	$FeCl_3$	water (0.08 ml)	1/90	80/0
6.	$FeCl_3$	water (0.08 ml)	8/90	25/75
7.	$FeCl_3.6H_2O$	neat	8/70	trace/90[b]
8.	$FeCl_3.6H_2O$	dichloroethane[c]	12/70	30/70
9	$FeCl_3.6H_2O$	dichloroethane[c]	15/28	40[d]
10	$FeCl_3.6H_2O$	1,4-dioxane	15/28	60/40
11.	$Cu(OTf)_2$	nitromethane	12/28	80/trace
12.	$CuCl_2$	nitromethane	12/28	80/trace
13.	$Cu(OAc)_2$	nitromethane	12/28	No reaction
14	TfOH	1,4-dioxane	12/28	70/0[e]
15	AcOH	neat	12/28 or 70	No reaction
16	p-TSA	nitromethane	12/60	80/0

[a]Reaction conditions: **1a** (1 equiv), **2a** (1 equiv) and acid (1 equiv) in a stoppered flask without exclusion of moisture/air using the LR grade solvent. [b]The ^{31}P NMR spectrum of reaction mixture showed the formation of **3b** in 98%. [c]nitromethane solvent also showed the same result. [d]remaining starting material (**1a**) was recovered. [e]The ^{31}P NMR spectrum for the reaction mixture showed another unassigned peak at δ22.1 (~30%).

The results shown in entries 1 and 7 (Table 1) incited us to perform the reaction using anhydrous $FeCl_3$ with two drops of water (0.08 ml) and that showed the consumption of both starting materials within 1 h at 90 °C to form compound **3a**. After 8h, **3a/3b** was isolated as a mixture in 1/3 ratio. The mixture of **3a** and **3b** was

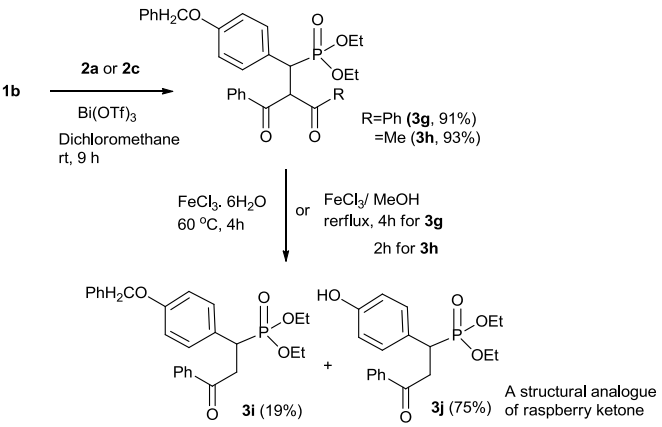
easily converted to only **3b** by treating with $FeCl_3.6H_2O$ at 60 °C for 5-6 h or by refluxing the mixture in the presence of $FeCl_3$ and methanol for 4 h. Although another C-C bond cleaved product, ester (**3b'**, Table 1) is expected from the reported Lewis acid mediated reactions of secondary alcohols and 1,3-diketones,[8] we could not find any product of type **3b'** during our investigations (verified by ^{31}P NMR spectrum[$] of the reaction mixture).

Being inexpensive and efficient Lewis acid, $FeCl_3.6H_2O$ was selected to run other reactions of phosphonate **1a** with diketones **2b-d** under solvent-free conditions at 70 °C but the reaction was not clean in case of symmetrical 1,3- diketone **2b**. The only phosphonylated 1,3-diketone (γ-ketophosphonate **3c**, Scheme 1) was obtained from the reaction of **2b** with **1a** at room temperature (28 °C) in dichloromethane (DCM) in the presence of anhydrous $FeCl_3$. No C-C bond cleaved product was obtained from **3c** even after repeated efforts under different reaction conditions. For both unsymmetrical 1,3-diketones **2c** and **2d**, phosphonate **1a** generated **3b** as a major regioselective C-C bond cleaved product in 80% and 95% yield respectively when $FeCl_3.6H_2O$ was used under neat conditions at 70 °C (Scheme 1). Although phosphonylated diketone **3d** was isolated in 16% yield from the reaction with **2c** but compound of type **3e** (Scheme 1, expected from **2d**) could not be isolated. This observation was even consistent for the reactions of other phosphonates **1b-e** with unsymmetrical 1,3-diketones like **2c-d**. The yield of **3d** was increased to ~90% by replacing $FeCl_3.6H_2O$ with anhydrous $FeCl_3$. The presence of -CF_3 group made the system comparatively more reactive to form the C-C bond cleaved product **3b** in 95% yield.



Scheme 1 Reaction of diketones **2b-d** with the α-hydroxyphosphonate **1a**.

The phosphonate **1b** generated a mixture of products (of type **3g, 3i** and **3j**; Scheme 2) from reactions with **2a** or **2c** under the same reaction conditions ($FeCl_3.6H_2O$, 8h, 70 °C). Attempt to use anhydrous $FeCl_3$ under neat conditions at 70 °C or in nitromethane at 28 °C also led to the same result. Gratifyingly, the use of $Bi(OTf)_3$ as a Lewis acid produced the 1,3-diketones **3g-h** in >90% yield (Scheme 2). Moreover, Fe(III) mediated regioselective bond cleavage for both compounds **3g-h** afforded expected compound **3i** (19%) as a minor product along with **3j** (75%) as a major product due to the favourable acid mediated O-CH_2Ph bond breakage. Compound **3h** was found to be more reactive compared to **3g** in terms of the C-C bond cleavage reaction. In this approach, *phenol functionality at α-carbon of γ-ketophosphonate* has been easily introduced by starting with **1b**. This ketone (**3j**) is a structural analogue of *raspberry ketone*,[11] a low-abundant natural product that contains a phenolic group.



Scheme 2 $Bi(OTf)_3$ mediated reaction of **1b** with 1,3-diketones **2a** or **2c**.

All other γ-ketophosphonates (**3k-u**), generated from reactions of α-hydroxyphosphonates (**1b-e)** and 1,3-diketones (**2a-d**) under different Lewis acids/reaction conditions have been presented in table 2 (for phosphonylated diketones) or table 3 (for phosphonylated monoketones).

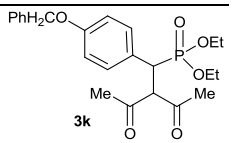
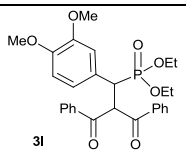
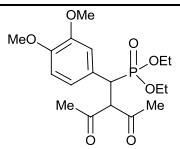
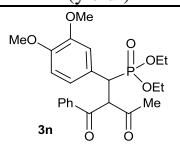
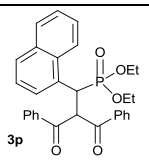
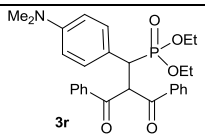
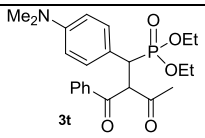
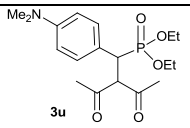
The phosphonylated 1,3-diketone (**3k**, entry 1, Table 2) was synthesised from reaction of phosphonate (**1b)** with acetylacetone (**2b**) by using anhydrous $FeCl_3$ in dichloromethane. In a similar manner, the reaction of **2b** with phosphonates **1c** and **1e** generated γ-ketophosphonate **3m†** (entry 3, Table 2) and **3u** (entry 8, Table 2) respectively. It is noted that the duration of reaction with phosphonates is comparatively higher for **2b** (18-30 h) than for other 1,3-diketones.

The ^{31}P NMR spectrum for the reaction mixture of Fe(III)-mediated reaction of phosphonate **1c** with 1,3-diketone **2c** showed the presence of two products that include phosphonylated 1,3-diketone **3n (**entry 4, Table 2, ~82% with a diastereomeric ratio 1:4) and monoketone **3o** (entry 1, Table 3, 18%). It was difficult to isolate these products in pure form. However, to our delight, use of $Cu(OTf)_2$ as a Lewis acid was successful to produce **3n (**entry 4, Table 2) in high yiled. The monoketone **3o** could also be obtained by using **1c** and **2d** in the presence of $FeCl_3.6H_2O$ (entry 1, Table 3). Again $Cu(OTf)_2$ worked well for synthesising phosphonylated diketone **3l** (entry 2, Table 2).

With the concern of synthesising useful reported compounds of type **A** (Fig. 1), our effort to use naphthalene based α-

hydroxyphosphonate **1d** gave a fruitful result with the reactions of 1,3-diketones (**2a-d)** to afford γ-ketophosphonates **3p** (phosphonylated 1,3-diketone, entry 5, Table 2) and **3q** (phosphonylated monoketone, entries 2 & 3, Table 3) in excellent yield using Fe(III) as Lewis acid. When the reaction between phosphonate **1d** and 1,3-diketone **2a** was performed using $FeCl_3.6H_2O$ under neat conditions at 70 °C, the reaction mixture showed the presence of diketone **3p** (5%) and regioselective C-C bond cleaved product monoketone **3q** (92%) in the ^{31}P NMR spectrum. The diketone **3p** was isolated in 72% yield by using anhydrous $FeCl_3$ in nitromethane after 16 h (entry 5, Table 2). The same reaction was also run using $Bi(OTf)_3$ but partial (~40%) conversion from **1d** to **3p** was observed, even after heating for 8 h. Both the unsymmetrical diketones **2c-d** generated compound **3q** in excellent yield (entry 3, Table 3) but corresponding phosphonylated 1,3-diketones were not isolated. Using this protocol, one can avoid using toxic halogenated and air/moisture sensitive compounds or pathways[1d] to synthesise *α*-naphthyl substituted *γ*-ketophosphonates (**3p-q)** efficiently. The acetylacetone (**2b**) was not reactive towards phosphonate **1d** to obtain the desired product under the present reaction conditions.

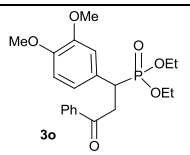
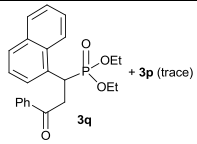
Table 2 Synthesis of phosphonylated 1,3-diketones (γ-ketophosphonates) from *α*-hydroxyphosphonates (**1b-e**) and 1,3-diketones (**2a-c**) under different reaction conditions[a]

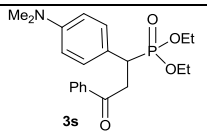
Entry	Phosphonates (**1**)/diketones (**2**)[a]	Lewis Acid/solvent/ temp (°C)/time (h)	γ-ketophosphonate (yield in %)
1	**1b/2b**	$FeCl_3$/ DCM /rt /18	 **3k** (83)
2	**1c/2a**	$Cu(OTf)_2$/nitromethane/ 60/ 8	 **3l** (88)
3.	**1c/2b**	$FeCl_3$/ DCM/ rt/ 30h	 **3m** (yield[b])
4	**1c/2c**	$Cu(OTf)_2$/ nitromethane/ 60/ 8h	 **3n** (81)
5	**1d/2a**	$FeCl_3$/ nitromethane/ rt/ 16h	 **3p** (72)
6	**1e/2a**[c]	$FeCl_3.6H_2O$/ neat/ 70/ 12	 **3r** (63)
7	**1e/2c**[d]	$FeCl_3.6H_2O$/neat/ 80/ 7	 **3t** (18%)
8	**1e/2b**	$FeCl_3$/DCM/rt/18h	 **3u** (89)

[a]Phosphonates (1 equiv), 1,3-diketone (1 equiv) and Lewis Acid (1 equiv). [b]**3m** was isolated along with **3ma** as a 1:1 mixture (see the experimental and supporting information for details).[c]The monoketone (**3s**, entry 4, Table 3) was isolated in 27% yield from this reaction. [d]The monoketone (**3s**) was isolated in 78% yield along with **3t.**

The *α*-dimethylamino substituted *γ*-ketophosphonates [phosphonylated 1,3-diketones **3r** and **3t-u** (entries 6-8, Table 2) and monoketone **3s** (entry 4, Table 3)] were obtained by starting from phosphonate **1e** and diketones **2a-d** using Fe(III)-mediated reactions. All these reactions were carried out under neat conditions at 70 °C except in case of synthesising **3u** as mentioned before. The reaction of **1e** with **2a** generated **3r** in 63% and **3s** in 27% yield where **2c** gave almost the same result like **2a** to afford compounds **3t** and **3s** (entry 7, Table 2) in 18% and 78% yields, respectively. Only phosphonylated monoketone **3s** was isolated when 1,3-diketone **2d** was used (entry 4, Table 3) for the reaction.

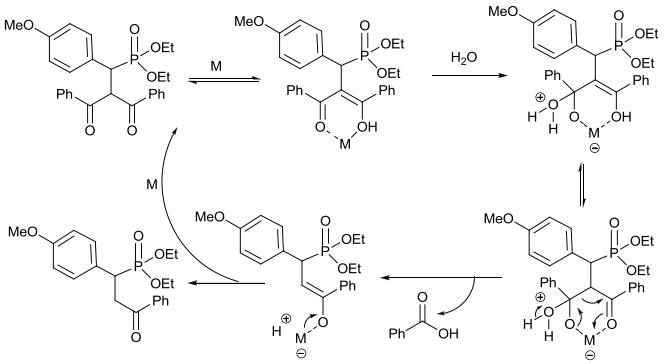
Table 3 Synthesis of phosphonylated monoketones (γ-ketophosphonates) from other *α*-hydroxyphosphonates (**1c-e**) and 1,3-diketones (**2a, 2c-d**) under different reaction conditions[a]

Entry	Phosphonates (**1**)/diketones (**2**)[a]	Acid/solvent/temp (°C)/time (h)	γ-ketophosphonate (yield in %)
1	**1c/2d**	$FeCl_3.6H_2O$/neat /60/8	 **3o** (93)
2	**1d/2a**	$FeCl_3.6H_2O$/neat /70/8	 **3q** + **3p** (trace) (91)

3.	**1d/2c or 2d**	$FeCl_3.6H_2O$/neat /70/12	**3q** (80)
4	**1e/2d**	$FeCl_3.6H_2O$/neat /70/12	 **3s** (91)

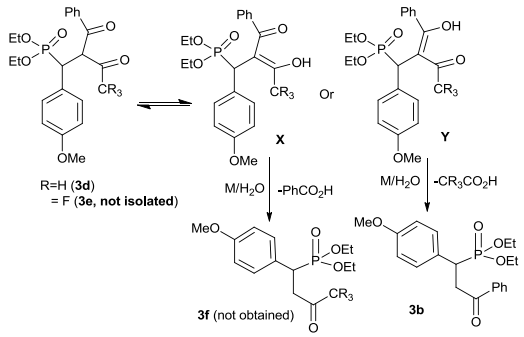
[a]Phosphonates (1 equiv), 1,3-diketone (1 equiv) and Lewis Acid (1 equiv).

From the literature survey[7,8] and the results obtained herein, the reaction mechanism could be explained by a direct alkylation of 1,3-diketones with a suitable carbocation obtained by the Lewis acid mediated activation of hydroxyl group (a poor leaving group) from α-hydroxyphosphonates. Generation of cations are subjective to the substituents (electron-donating/ extended conjugation) present in the benzene ring. Furthermore, nucleophilic reaction might depend on the keto/enol ratio including the steric factor of the 1,3-diketones. Notably, 1,3-diketones are also known to act as bidentate ligands to decrease the Lewis acidity of the metals.[7d] Along with that, the subsequent regioselective C-C bond cleavage is also a reason to stabilise the best reaction conditions for different combinations of α-hydroxyphosphonates and 1,3-diketones to afford the desired γ-ketophosphonates. Moreover, with all these experimental results, we believe the C-C bond cleavage occurs with the help of water molecules present in the reaction mixture. Based on the literature,[8] proposed metal mediated C-C bond cleavage mechanism (Scheme 3) predicts the formation of benzoic acid that was successfully isolated in sublimed form from the wall of the reaction flask. With this result, helpful evidence is established for the proposed mechanism which has not been demonstrated so far due to the formation of volatile ester as a side product because alcohol was used in place of water.[8]



Scheme 3 Proposed pathway for the C-C bond cleavage

With the experimental observations obtained from the reactions of unsymmetrical 1,3-diketones and considering the stability of the possible tautomeric forms (**X** and **Y**, Scheme 4) we surmise that the more conjugated enol form **Y** is the most favourable one to obtain the product **3b** under the present reaction condition.



Scheme 4 The reaction of **1a** with unsymmetrical 1,3-diketones.

A theoretical calculation considering **3d** showed a small difference in energy between the form **X** and **Y**.[12] The product of type **3f** was not formed under these reaction conditions. In the literature, enol form of type **X** was considered to be the most stable one based on the experimental observations.[8c-d]

Conclusions

This study describes a new convenient and inexpensive method to synthesise a variety of biologically important γ-ketophosphonates in good yields. The reaction conditions are optimised for different combinations of α-hydroxyphosphonates and 1,3-diketones to generate the desired compounds effectively. Fe(III) is the Lewis acid of choice to generate most of the phosphonylated di/monoketones. Only for generating phosphonylated diketones **3g-h,** $Bi(OTf)_3$ was used and $Cu(OTf)_2$ was chosen to synthesise posphonylated diketones **3l & 3n.** The Lewis acid $FeCl_3.6H_2O$ is successfully used for the C-C bond cleavage reactions to synthesise phosphonylated monoketones. Finally, we are able to accomplish the synthesis of the structural analogue of raspberry ketone.

Experimental

Silica gel (100-120 mesh size) was used for the column chromatography. Reactions were monitored by TLC on silica gel 60 F254 (0.25 mm). ^1H, ^{13}C, and ^{31}P NMR spectra (^1H, 400 or 500 MHz; ^{13}C, 101 or 125 MHz; ^{31}P, 162 or 212 MHz) were recorded using a 400 or 500 MHz spectrometer in $CDCl_3$ with shifts referenced to $SiMe_4$ (δ 0) or 85% H_3PO_4 (δ 0). Some cases (for compounds **3m+3ma, 3k and 3j**) DEPT experiments were also performed. IR spectra were recorded on an FT-IR spectrophotometer. Melting points were determined by using a local hot-stage melting point apparatus and were uncorrected. Elemental analyses were carried out on a CHN analyzer. Mass spectra were recorded using LC-MS equipment. Compounds diethyl hydroxyl(aryl)methylphosphonates **1a-e** were prepared by following methods reported in the literatures.[9] Reactions were run without exclusion of air/moisture in a stoppered reaction flask.

(i) Reaction of 1a with 1,3-diketone (2a):

Synthesis of (±)-diethyl 2-benzoyl-1-(4-methoxyphenyl)-3-oxo-3-phenylpropylphosphonate (3a) To a stirred solution of **1a** (0.50 g, 1.82 mmol), dibenzoylmethane (**2a**, 0.400 g, 1.82 mmol), anhydous

$FeCl_3$ (0.29 g, 1.82 mmol) was added and then the reaction mixture was heated at 70°C for 8 h. After completion of the reaction as indicated by TLC, the reaction was quenched with saturated NH_4Cl solution. The aqueous layer was extracted with ethyl acetate (3 x 20 ml). After filtration and removal of solvent in vacuum, the crude product was purified by column chromatography using EtOAc/ pet ether (70/30) as the eluent to afford **3a.** Yield 0.788 g (90%); off-white solid; mp 172-174 °C; IR (KBr, cm^{-1}) 2983, 1700, 1602, 1508, 1257, 1024, 966; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.93-0.97 (m, 6H), 3.45-3.69 (m, 1H), 3.72 (s, 3H), 3.74-3.87 (m, 3H), 4.45 (dd, *J* = 19.7 and 11.3 Hz, 1H), 6.42 (dd, *J* = 11.1 and 10.0 Hz, 1H), 6.69-6.72 (m, 2H), 7.24-7.34 (m, 2H), 7.41-7.59 (m, 6H), 7.75 (d, *J* = 8.6 Hz, 2H), 8.20 (d, *J* = 7.2 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 15.9 and 16.1 (d, *J* ~ 6.0 Hz each), 44.2 (d, *J* = 139.1 Hz), 55.2, 56.9, 61.9 and 63.5 (d, *J* = 7.3 Hz each), 113.9, 125.8 (d, *J* = 7.0 Hz), 128.6 (d, *J* = 4.5 Hz),, 128.9, 129.3, 131.2 (d, *J* = 6.4 Hz), 133.4, 133.6, 136.9, 137.0, 158.8, 192.2 (d, *J* = 16.5 Hz), 192.9; ^{31}P NMR (162 MHz, $CDCl_3$) δ 27.0 (s); LC/MS m/z 481 $[M+H]^+$; Anal. Calcd. for $C_{27}H_{29}O_6P$ C 67.49, H 6.08; found C 67.58, H 6.14.

(±)-Diethyl 1-(4-methoxyphenyl)-3-oxo-3-phenylpropylphosphonate (3b) This compound was synthesised in a manner similar to the synthesis of **3a** with similar molar quantities using $FeCl_3$. $6H_2O$. Yield 0.618 g (90%); viscous liquid; IR (KBr, cm^{-1}) 2983, 1686, 1605, 1510, 1450, 1246, 1034, 959; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.10 and 1.29 (two sets of triplet, *J* ~ 7.1 Hz each, 6H), 3.61-3.73 (m, 3H), 3.76 (s, 3H), 3.89-3.91 (m, 2H), 3.94-4.12 (m, 2H), 6.84 (d, *J* = 8.0 Hz, 2H), 7.35-7.37 (m, 2H), 7.43-7.56 (m, 3H), 7.94 (d, *J* = 7.2 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 16.3 and 16.4 (two sets of doublets, *J* = 5.0 Hz each), 38.1 (d, *J* = 138 .0Hz), 39.2, 55.2, 61.9 and 62.9 (two sets of doublets, *J* = 7.5 Hz each), 113.9 (d, *J* = 2.5 Hz), 127.8 (d, *J* = 6.2 Hz), 128.1, 128.6, 130.2 (d, *J* = 7.5 Hz), 133.3, 136.6, 158.7 (d, *J* = 2.5 Hz), 196.5 (d, *J* = 15.0 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 28.9. LC/MS m/z 377 $[M+H]^+$. This compound is reported in the literature.[5d]

(ii) Reactions of 1a with 1,3-diketones (2b-d)

Synthesis of (±)-diethyl 2-acetyl-1-(4-methoxyphenyl)-3-oxobutylphosphonate (3c) To a stirred solution of **1a** (0.50 g, 1.82 mmol) and acetylacetone (**2b**, 0.18 g, 1.82 mmol), in anhydrous dichloromethane (4 mL) as solvent, anhydrous $FeCl_3$ (0.29 g, 1.82 mmol) was added and then the reaction mixture was stirred at 28 °C for 18 h**.** The compound **3c** was isolated using column chromatography (EtOAc/Hexane) with partial (~14%) enol form. Yield 0.590g, (91%); off-white solid; mp 192-194 °C; IR (KBr, cm^{-1}) 2356, 1690, 1515, 1361, 1265, 1176, 1026, 937; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.08 and 1.23 (two sets of triplet, *J* ~ 7.2 Hz each, 6H), 1.81 (s, 3H), 2.33 (s, 3H), 3.64-3.74 (m, 1H), 3.76 (s, 3H), 3.82 – 4.04 (m, 4H), 4.59 (dd→t, *J* = 11.4 and 11.6 Hz, 1H), 6.81 (d, *J* = 8.8 Hz, 2H), 7.17-7.19 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 16.2 and 16.3 (d, *J* ~ 6.0 Hz each), 28.2, 30.6, 43.1 (d, *J* = 138.9 Hz), 55.3, 62.5 and 63.2 (d, *J* = 7.0 Hz each), 69.5, 114.3, 124.9 130.8, 159.2, 201.5, 201.7 (d, *J* = 17.7 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 25.6 (s); LC/MS m/z 357 $[M+H]^+$; Anal. Calcd. for $C_{17}H_{25}O_6P$ C 57.30, H 7.07; found C 57.42, H 6.87.

Synthesis of (±)-diethyl 2-benzoyl-1-(4-methoxyphenyl)-3-oxobutylphosphonate (3d) Reaction was performed in a manner similar to the synthesis of **3b** using benzoylacetone (**2c**) with a similar quantity as **2a**. The product **3d** (0.534 g, yield 16%) was isolated followed by **3b** (0.550g, yield 80%). Under the same reaction conditions ($FeCl_3.6H_2O$, neat, 70 °C, 80 h), the reaction of **1a** with **2d** gave exclusively compound **3b** in 95% yield. The yield of **3d** was increased to 90% by performing the reaction using anhydrous $FeCl_3$.

Characterization for **3d:** off-white solid; mp 96-98 °C; IR (KBr, cm^{-1}) 2980, 1726, 1680, 1511, 1253, 1028, 960; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.96 and 1.02 (two sets of triplet, *J* ~ 7.0 Hz each, 6H), 1.83 (s, 3H), 3.56-3.88 (m, 7H, the singlet at δ 3.73 was also merged), 4.31 (dd, *J* = 21.6, 11.8 Hz, 1H), 5.49 (dd→t, *J* = 9.6 and 11.6 Hz, 1H), 6.86 (d, *J* = 8.4 Hz, 2H), 7.32-7.34 (m, 2H), 7.48-7.62 (m, 3H), 8.15 (d, *J* = 7.5 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 16.0 and 16.1 (d, *J* ~ 5.6 Hz each), 27.5, 43.5 (d, *J* = 137.5 Hz), 55.3, 62.3 and 63.2 (d, *J* = 7.0 Hz each), 63.6, 114.3, 124.9, 128.9, 129.2, 131.2, 133.9, 136.6, 159.2, 193.4, 201.7 (d, *J* = 17.5 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 25.8 (s); LC/MS m/z 419 $[M+H]^+$; Anal. Calcd. for $C_{22}H_{27}O_6P$ C 63.15, H 6.50; found C 62.89, H 6.72.

(iii) Reactions of 1b with 1,3-diketones (2a&2c)

Synthesis of (±)-diethyl 2-benzoyl-1-(4-(benzyloxy)phenyl)-3-oxo-3-phenylpropylphosphonate (3g) To a stirred solution of **1b** (0.50 g, 1.42 mmol) and dibenzoylmethane (**2a**, 0.31 g, 1.42 mmol), in anhydrous dichloromethane (4 mL) as solvent, $Bi(OTf)_3$ (0.46 g, 0.70 mmol) was added and then the reaction mixture was stirred at rt for 9 h**.** The compound was isolated using column chromatography. Yield 0.720 g, (91%); off-white solid; mp 170-172 °C; IR (KBr, cm^{-1}) 2987, 1695, 1602, 1510, 1445, 1253, 1026, 954; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.95-1.03 (m, 6H), 3.47-3.57 (m, 1H), 3.72-3.93 (m, 3H), 4.49 (dd, J = 22 Hz, 12 Hz, 1H), 4.97 (s, 2H), 6.42-6.47 (m, 1H), 6.82 (d, *J* = 8.0 Hz, 2H), 7.2-7.49 (m, 10H), 7.50-7.62 (m, 3H), 7.78 (d, *J* = 8.0 Hz, 2H) 8.24 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 15.8 and 16.0 (two sets of doublets, *J* = 6.1 Hz each), 44.2 (d, *J* = 139.4 Hz), 56.9, 61.9 and 63.3 (two sets of doublets, *J* = 7.1 Hz each), 69.9, 114.8, 114.9, 126.1 (d, *J* = 7.0 Hz), 127.5, 127.9, 128.5, 128.6, 128.8, 129.2,131.2, 133.3, 133.5, 136.8, 136.9, 158.0, 192.2 (d, *J* = 17.2 Hz), 192.9; ^{31}P NMR (162 MHz, $CDCl_3$) δ 26.3; LC/MS m/z 557 $[M+H]^+$; Anal. Calcd for $C_{33}H_{33}O_6P$ C, 71.21; H, 5.98; Found C, 71.28 H, 5.83.

Synthesis of (±)-diethyl 2-benzoyl-1-(4-(benzyloxy)phenyl)-3-oxobutylphosphonate (3h) By starting with **2c**, this compound was synthesised using similar procedure and molar quantities as **3g.** Yield 0.650 g, (93%); viscous liquid; IR (KBr, cm^{-1}) 1723, 1680, 1602, 1508, 1450, 1253, 1035, 969; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.98 and 1.04 (two sets of triplet, *J* = ~7.5 Hz each, 6H), 1.86 (s, 3H), 3.59-3.89 (m, 4H), 4.37 (dd, *J* = 24 Hz, 12 Hz, 1H), 5.06 (s, 2H), 4.53 (dd→t, *J* = 12.0 Hz each, 1H), 6.97 (d, *J* = 8.0 Hz, 2H), 7.34-7.65 (m, 10H), 8.18 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 15.9 and 16.0 (two sets of doublets, *J* = 6.1 Hz each), 27.4, 43.5 (d, *J* = 138.4 Hz), 62.1 and 63.1 (two sets of doublets, *J* = 7.1 Hz each), 63.5, 70.1, 115.2 (d, *J* = 3.0 Hz), 125.3 (d, *J* = 8.0 Hz), 127.6, 128.0, 128.6, 128.8, 129.1, 131.2 (d, *J* = 6.0 Hz), 133.8, 136.6, 136.8, 158.4 (d, *J* = 3.0 Hz), 193.3, 201.5 (d, *J* = 18.0 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 25.2. LC/MS m/z 495 $[M+H]^+$; Anal. Calcd for $C_{28}H_{31}O_6P$ C, 68.01; H, 6.32. Found C, 68.15; H, 6.26.

(iv) Regioselective C-C bond cleavage for 3g and 3h: **Synthesis of 3i and 3j**: A solution of **3h** (0.40 g, 0.81 mmol) in methanol was heated under reflux using $FeCl_3$ (0.13 g, 0.81 mmol) for 2 h. The compound **3i** was isolated using column chromatography followed by **3j**. In case of **3g,** the reaction mixture had to stir for 4h. The same result was also obtained by using $FeCl_3.6H_2O$ at 60 °C for 6h.

(±)-Diethyl (1-(4-(benzyloxy)phenyl)-3-oxo-3-phenylpropyl)phosphonate (3i) Yield 0.071g, (19%); viscous liquid; IR (KBr, cm^{-1}) 2925, 1687, 1604, 1508, 1445, 1225, 1025, 969; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.08 and 1.28 (two sets of triplet, *J* =6.8 Hz each, 6H), 3.58-3.74 (m, 3H), 3.87-3.97 (m, 2H),

4.01-4.11 (m, 2H), 5.00 (s, 2H), 6.89 (d, *J* = 8.8 Hz, 2H), 7.29-7.56 (m, 10H), 7.92 (d, *J* = 7.6 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 16.3 and 16.5 (two sets of doublets, *J* = 6.1 Hz each), 38.2 (d, *J* = 142.0 Hz), 39.3, 62.1 and 63.1 (two sets of doublets, *J* = 7.1 Hz each), 70.1, 114.9, 127.6, 128.0, 128.2, 128.6, 128.7, 130.3, 130.4, 133.4, 136.7, 137.0, 158.1 (d, *J* = 2.7 Hz), 196.6 (d, *J* = 15.6 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 29.5; LC/MS m/z 453 $[M + H]^+$.

(±)-Diethyl 1-(4-hydroxyphenyl)-3-oxo-3-phenylpropylphosphonate (3j) Yield 0.220 g, (75%); off-white solid; mp 114-116 °C; IR (KBr, cm^{-1}) 3207, 1686, 1604, 1512, 1450, 1229, 1027, 975; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.10 and 1.27 (t, *J* = 7.0 Hz each , 6H), 3.55-3.79 (m, 3H), 3.85-3.94 (m, 2H), 4.02-4.09 (m, 2H), 6.61 (d, *J* = 8.5 Hz, 2H), 7.15-7.17 (m, 2H), 7.40-7.54 (m, 3H), 7.90- 7.93 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 16.3 and 16.4 (two sets of doublets, *J* = 5.8 Hz each), 38.1 (d, *J* = 141.5 Hz), 38.9, 62.3 and 63.3 (two sets of doublets, *J* = 7.3 Hz each), 116.0, 125.9 (d, *J* = 7.2 Hz), 128.2, 128.7, 130.2, 133.4, 136.6, 156.2, 196.8 (d, *J* = 14.5 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 29.7. LC/MS m/z 363 $[M + H]^+$; Anal. Calcd for $C_{19}H_{23}O_5P$ C, 62.98; H, 6.40. Found C, 63.17; H, 6.51.

(v) Reactions of 1b with 1,3-diketone (2b): **Synthesis of (±)-diethyl 2-acetyl-1-(4-(benzyloxy)phenyl)-3-oxobutylphosphonate (3k).** This compound is synthesised in a manner analogous to compound **3c** by starting with **1b** (0.50 g) using similar molar quantitites. Yield 0.510 g, (83%); off-white solid; mp 118-120 °C; IR (KBr, cm^{-1}) 2984, 1696, 1607, 1512, 1360, 1244, 1029, 965; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.09 and 1.24 (two sets of triplet, *J* = 7.2 Hz each, 6H), 1.83 (s, 3H), 2.34 (s, 3H), 3.63-3.71 (m, 1H), 3.81-4.05 (m, 4H), 4.60 (dd→t, *J*~ 11.6 Hz each, 1H), 5.01 (s, 2H), 6.90 (d, *J* = 8.8 Hz, 2H), 7.18- 7.21 (m, 2H), 7.30-7.41 (m, 5H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 16.2 and 16.3 (two sets of doublets, *J* = 5.5 Hz each), 28.2, 30.5, 43.1 (d, *J* = 138.1 Hz), 62.5 and 63.2 (two sets of doublets, *J* = 7.1 Hz each), 69.5, 70.1, 115.3, 125.4 (d, *J* = 7.8 Hz), 127.6, 128.1, 128.7, 130.8 (d, *J* = 5.7 Hz), 136.8, 158.4, 201.5, 201.7 (d, *J* = 17.7 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 25.6. LC/MS m/z 433 $[M + H]^+$; Anal. Calcd for $C_{23}H_{29}O_6P$ C, 63.88; H, 6.76. Found C, 63.94; H, 6.49.

(vi) Reaction of 1c with 1,3-diketone 2a: **Synthesis of (±)-diethyl 2-benzoyl-1-(3,4-dimethoxyphenyl)-3-oxo-3-phenylpropylphosphonate (3l)** To a stirred solution of **1c** (0.50 g, 1.64 mmol), dibenzoylmethane (0.36 g, 1.64 mmol) in anhydrous nitromethane (4 mL) as solvent, copper(II) trifluoromethanesulfonate (0.59 g, 1.63 mmol) was added and then the reaction mixture was stirred at 60°C for 8 h**.** The compound **3l** was isolated using column chromatography. Yield 0.740 g, (88%); off-white solid; mp 147-149 °C; IR (KBr, cm^{-1}) 2983, 1693, 1589, 1515, 1452, 1258, 1153, 1034, 962; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.94-1.00 (m, 6H) 3.46-3.54 (m, 1H), 3.73 (s, 3H),3.76-3.91 (m, 6H), 4.45 (dd, *J* = 19.8 and 11.1 Hz, 1H), 6.44 (dd→t, *J* = 11.1 and 10.0 Hz, 1H), 6.66 (d, *J* = 8.3 Hz, 1H), 6.92-6.98 (m, 2H), 7.25-7.29 (m, 2H), 7.39-7.58 (m, 4H), 7.77 (d, *J* = 7.5 Hz, 2H), 8.19 (d, *J* = 7.5 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 15.9 and 16.2 (d, *J* ~ 5.9 Hz each), 44.6 (d, *J* = 138.7 Hz), 55.7, 55.8, 56.7, 57.4, 61.9 and 63.5 (d, *J* = 7.2 Hz each), 110.9 (d, *J* = 1.6 Hz), 113.3 (d, *J* = 6.0 Hz), 122.6 (d, *J* = 7.0 Hz), 126.0 (d, *J* = 6.6 Hz), 128.6, 128.7, 128.9, 129.2, 133.4, 133.6, 136.9, 127.1, 148.2, 148.6, 192.3 (d, *J* = 16.1 Hz), 192.8; ^{31}P NMR (162 MHz, $CDCl_3$) δ 27.0 (s); LC/MS m/z 511 $[M + H]^+$; Anal. Calcd for $C_{28}H_{31}O_7P$ C, 65.87; H, 6.12. Found C, 65.94; H, 6.03.

(vii) Reaction of acetylacetone (2b) with 1c: This reaction was performed in a manner analogous to synthesis of compound **3c** by starting with **1c** (0.50 g, 1.42mmol) using similar molar quantitites at 28 °C for 24 h**.** The compound **3m** was isolated along with **3ma** in 1:1 ratio. The amount isolated from column 0.55 g (mixture of **3m** & **3ma**), The compound **3ma** (0.25 g, 44 %) was crystalised from this mixture from dichloromethane/hexane mixture (1:2).

Spectroscopic data for the mixture of **3m** & **3ma**:

IR (KBr, cm^{-1}) 2989, 1697, 1658, 1350, 1242, 1030, 964; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.01 and 1.18 (two sets of triplet, *J* = 7.2 Hz each, 6H), 1.81 (s, 3H), 2.28 and 2.32 (s, 3H), 3.58-3.65 (m, 1H), 3.70-3.82 (m, 2H), 3.79 & 3.81 (s, each 3H), 3.86-4.03 (m, 1H), 4.49-4.55 (m, 1H), 4.61 (dd→t, *J*~ 11.4 &11.6 Hz each, 1H), 6.75-6.81 (m, 3H); Peaks for **3ma** appeared at δ 1.09 and 1.23 (two sets of triplet, *J* = 7.2 Hz each, 6H), 2.44 (dd, *J*~ 1.9 & 5.4 Hz, 3H), 2.48 (s, 3H), 3.58-3.68 (m, 1H), 3.84-3.88 (m, 1H), 3.93 (s, 6H), 4.01-4.06 (m, 2H), 4.42-4.49 (qd, *J* = 2 &29.5 Hz, not well resolved, 1H), 6.96 (s,1H), 7.32 (d, *J* = 1.6 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 16.2 and 16.3 (d, *J* ~ 5.7 Hz each), 28.2, 30.6, 43.5 (d, *J* = 138.7 Hz), 55.8, 56.1, 62.5 and 63.3 (d, *J* = 7.2 Hz each), 69.5, 111.2 (d, *J* = 2.3 Hz), 112.7 (d, *J* = 5.1 Hz), 122.0 (d, *J* = 6.4 Hz), 125.4 (d, *J* = 7.9 Hz), 148.6 (d, *J* = 2.3 Hz), 149.0 (d, *J* = 2.5 Hz), 150.6 (d, *J* = 9.6 Hz); Peaks for **3ma** appeared at δ 13.2, 16.3 (d, *J* ~ 6.1 Hz), 31.0, 49.7 (d, *J* = 131.2 Hz), 56.0, 56.3, 62.9 and 63.1 (d, *J* = 7.2 Hz each), 104.1, 108.5, 132.5 (d, *J* = 6.2 Hz), 135.0 (d, *J* = 8.2 Hz), 137.9 (d, *J* = 4.4 Hz), 149.7, 150.1 (d, *J* = 2.1 Hz),196.8; ^{31}P NMR (162 MHz, $CDCl_3$) δ 25.6 (s) & 23.9 (s) (1:1); LC/MS m/z 387 [M + H] for **3m** and 369 $[M + Na + 2H]^+$ for **3ma**.

Data for the 3ma obtained after crystallization

White crystalline solid; mp 126-128 °C; IR (KBr, cm^{-1}) 2989, 1656, 1555, 1338, 1243, 1031, 965; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.06 and 1.23 (two sets of triplet, *J* = 7.2 Hz each, 6H), 2.44 (dd, *J*~ 2.0 & 5.5 Hz, 3H), 2.53 (s, 3H), 3.62-3.68 (m, 1H), 3.84-3.88 (m, 1H), 3.97 (s, 6H), 4.01-4.06 (m, 2H), 4.46-4.53 (qd, *J* = 2.0 & 29.5 Hz, not well resolved, 1H), 7.00 (s,1H), 7.37 (d, *J* = 2.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.0, 16.2 (d, *J* ~ 6.2 Hz), 30.9, 49.7 (d, *J* = 130.0 Hz), 56.1, 56.2, 62.9 and 63.1 (d, *J* = 7.2 Hz each), 104.1, 108.5, 132.5 (d, *J* = 6.2 Hz), 135.0 (d, *J* = 8.2 Hz), 137.9 (d, *J* = 4.4 Hz), 149.7, 150.0, 196.7. ^{31}P NMR (162 MHz, $CDCl_3$) δ 23.3 (s) [96%]; ~4% of **3m** also was observed in ^{31}P NMR]. LC/MS m/z 369 $[M + Na + 2H]^+$; Anal. Calcd. for $C_{16}H_{25}O_6P$ C 55.81, H 7.32; found C 56.19, H 6.35.

(viii) Reaction of 1c with 1,3-diketones 2c and 2d: **Synthesis of (±)-diethyl (2-benzoyl-1-(3,4-dimethoxyphenyl)-3-oxobutyl)phosphonate (3n)** Similar procedure and molar quantities as **3l** are used. The reaction mixture of **1c** and **2c** was stirred at 60 °C for 6h. Yield 0.600 g, (81%); viscous liquid; IR (KBr, cm^{-1}) 2986, 1722, 1679,1589, 1513, 1254, 1023; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.96 and 1.01 (two sets of triplet, *J* = 7.0 Hz each, 6H), 1.83 (s, 3H), 3.56-3.82 (m, 4H), 3.85 (s, 3H), 3.90 (s, 3H), 4.31 (dd, *J* = 21.7 and 11.7 Hz, 1H), 5.51 (dd→t, *J* = 11.9 and 12.0 Hz, 1H), 6.81 (d, *J* = 8.0 Hz, 1H), 6.92-6.96 (m, 2H), 7.48-7.62 (m, 3H), 8.14-8.16 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 16.1 and 16.2 (d, *J* ~ 6.0 Hz each), 27.5, 43.8 (d, *J* = 138.3 Hz), 55.8, 55.9, 62.2 and 63.2 (d, *J* = 7.6 Hz each), 63.6, 11.2, 113.2, 122.5 (d, *J* = 7.1 Hz), 125.4 (d, *J* = 7.9 Hz), 128.9, 129.2, 133.9, 136.6, 148.7 (d, *J* = 3.3 Hz), 149.0 (d, *J* = 2.2 Hz), 193.3, 201.7 (d, *J* = 17.4 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 25.8 (s); LC/MS m/z 449 $[M + H]^+$; Anal. Calcd for $C_{23}H_{29}O_7P$ C, 61.60; H, 6.52. Found C, 61.38; H, 6.26.

Synthesis of (±)-diethyl (1-(3,4-dimethoxyphenyl)-3-oxo-3-phenylpropyl)phosphonate (3o). This compound was synthesised using similar procedure and molar quantities as **3b** for 8 h from the reaction of **1c** with **2d.** Yield 0.620 g, (93%); viscous liquid; IR (KBr, cm^{-1}) 2983, 1685, 1593, 1514, 1253, 1152, 1033; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.09 and 1.27 (two sets of triplet, *J* ~ 6.8 Hz

each, 6H), 3.57-3.73 (m, 3H), 3.75 (s, 3H), 3.82 (s, 3H), 3.88-3.94 (m, 2H), 4.05-4.09 (m, 2H), 6.77 (d, *J* = 8.0 Hz, 1H), 6.95-6.98 (m, 2H), 7.41-7.45 (m, 2H), 7.52-7.56 (m, 1H), 7.93 (d, *J* = 9.6 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 16.3 and 16.4 (two sets of doublets, *J* = 6.1 Hz each), 38.5 (d, *J* = 141.4 Hz), 39.3, 55.8, 55.9, 61.9 and 62.9 (two sets of doublets, *J* = 7.1 Hz each), 111.1 (d, *J* = 3.0 Hz), 112.6 (d, *J* = 6.1 Hz), 121.4 (d, *J* = 7.1 Hz), 128.1, 128.2 (d, *J* = 7.1 Hz), 128.6, 133.3, 136.6, 148.2 (d, *J* = 3.0 Hz), 148.7 (d, *J* = 3.0 Hz), 196.5 (d, *J* = 15.1 Hz);; ^{31}P NMR (162 MHz, $CDCl_3$) δ 28.8. LC/MS m/z 407 $[M + H]^+$; Anal. Calcd for $C_{21}H_{27}O_6P$ C, 62.06; H, 6.70. Found C, 61.86; H, 6.48.

(ix) Reaction of 1d with 1,3-diketones 2a, 2c and 2d

Synthesis of (±)-diethyl 2-benzoyl-1-(naphthalene-1-yl)-3-oxo-3-phenylpropylphosphonate (3p) To a stirred solution of **1d** (0.50 g, 1.7 mmol) and dibenzoylmethane (**2a**, 0.38 g, 1.7 mmol), in anhydrous nitromethane (4 mL) as solvent, anhydrous $FeCl_3$ (0.27 g, 1.7 mmol equiv) was added and then the reaction mixture was stirred at 28 °C for 16 h**.** Yield 0.610 g, (72%); off-white solid; mp 186-188; IR (KBr, cm^{-1}) 2982, 1706, 1589, 1445, 1257, 1241, 1016, 969; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.58 and 0.97 (two sets of triplet, *J* = 7.1 Hz each, each 3H), 3.01-3.08 (m, 1H), 3.49-3.58 (m, 1H), 3.69-3.89 (m, 2H), 5.46 (dd, *J* = 20.5 and 11.0 Hz, 1H), 6.69 (dd→t, *J* = 11.1 and 10.0 Hz, 1H), 7.17-7.26 (m, 3H), 7.31-7.35 (m, 1H), 7.44-7.54 (m, 3H), 7.58-7.77 (m, 7H), 8.29-8.31 (m, 2H), 8.46 (d, *J* = 8.6 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 15.7 and 15.9 (d, *J* ~ 6.0 Hz each), 38.7 (d, *J* = 138.6 Hz), 57.4, 62.0 and 63.5 (d, *J* = 7.2 Hz each), 124.1, 124.7 (d, *J* = 3.3 Hz), 125.9, 126.6 (d, *J* = 4.7 Hz), 128.2 (d, *J* = 3.2 Hz), 128.5, 128.6 (d, *J* = 5.7 Hz), 128.9, 129.4, 130.7 (d, *J* = 6.6 Hz), 132.6, 132.65, 133.2, 133.7, 133.9, 136.8, 137.0, 191.9 (d, *J* = 16.0 Hz), 193.2; ^{31}P NMR (162 MHz, $CDCl_3$) δ 27.1 (s); LC/MS m/z 501 $[M + H]^+$; Anal. Calcd for $C_{30}H_{29}O_5P$ C, 71.99; H, 5.84. Found C, 72.13; H, 5.76. This compound is reported in the literature.[1d]

(±)-Diethyl 1-(naphthalene-1-yl)-3-oxo-3-phenylpropylphosphonate (3q) This compound was synthesised using similar procedure and molar quantities as **3b** for 8 h using the diketone **2a.** Yield 0.610g, (91%); viscous liquid; IR (KBr, cm^{-1}) 1684, 1236, 1026, 959; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.78 and 1.25 (two sets of triplet, *J* ~ 8 Hz each, each 3H), 3.35-3.44 (m, 1H), 3.68-3.76 (m, 1H), 3.90-3.93 (m, 2H), 4.05-4.10 (m, 2H), 4.91-4.95 (m, br, 1H), 7.39-7.42 (m, 3H), 7.43-7.50 (m, 2H), 7.53-7.58 (m, 1H), 7.60-7.74 (m, 2H), 7.82 (d, *J* = 8.0 Hz, 1H), 7.94 (d, *J* = 8.0 Hz, 2H), 8.38 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 16.0 and 16.4 (two sets of doublets, *J* = 5.5 Hz each), 32.7 (d, *J* = 135.5 Hz), 40.2, 62.2 and 63.1 (two sets of doublets, *J* = 7.2 Hz each), 123.7, 125.2, 125.3, 125.8, 126.5, 127.9, 128.2, 128.7, 128.8, 132.3 (d, *J* = 6.1 Hz), 132.7 (d, *J* = 6.1 Hz), 133.4, 133.9, 136.6, 196.6; ^{31}P NMR (162 MHz, $CDCl_3$) δ 29.5; LC/MS m/z 397 $[M + H]^+$; Anal. Calcd for $C_{23}H_{25}O_4P$ C, 69.69; H, 6.36. Found C, 69.74; H, 6.27. This compound is also reported.[5d]

The other diketones **2c** and **2d** also produced **3q** in 80% yield under the same reaction conditions after 12 h.

(x) The reaction of phosphonate 1e with diketones 2a, 2c and 2d : The reaction was performed in a manner analogous to the reaction for synthesizing **3b** using similar molar quantities**.** The compound **3r** (yield 0.540 g, 63%; off-white solid. mp 170-172 °C) was isolated followed by **3s** (yield 0.180, 27%; viscous liquid) using column chromatography. In case of **2c**, reaction mixture was stirred at 80 °C for 7 h to produce **3t [**Yield: 0.130g, (18%), light brown solid] and **3s** [Yield: 0.530 g, (78%); viscous liquid]. For **2d**, the reaction mixture was stirred at 70 °C for 12 h to afford **3s** with isolated yield 0.610 g (91%).

(±)-Diethyl 2-benzoyl-1-(4-(dimethylamino)phenyl)-3-oxo-3-phenylpropylphosphonate (3r) IR (KBr, cm^{-1}) 1696, 1605, 1522, 1253, 1050, 965; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.96-0.98 (m, 6H), 2.84 (s, 6H), 3.47-3.53 (m, 1H), 3.79-3.88 (m, 3H), 4.42 (dd, *J* = 19.7 and 11.3 Hz, 1H), 6.45 (dd→t, *J* = 12 and 8.0 Hz, 1H), 6.55 (d, *J* = 8.5 Hz, 2H), 7.25- 7.38 (m, 4H), 7.56-7.59 (m, 4H), 7.79 (d, *J* = 7.9 Hz, 2H), 8.23 (d, *J* = 7.8 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 15.9 and 16.2 (d, *J* = 6.1 Hz), 40.4, 44.1 (d, *J* = 139.4 Hz), 56.8, 61.7 and 63.4 (d, *J* = 7.2 Hz), 112.5, 120.9 (d, *J* = 7.2 Hz), 128.5, 128.6, 128.7, 129.2, 130.6 (d, J = 6.1 Hz), 133.1, 133.4, 137.0, 149.7, 192.3 (d, *J* = 16.7 Hz), 193.1; ^{31}P NMR (212 MHz, $CDCl_3$) δ 26.8 (s); LC/MS m/z 494 $[M + H]^+$; Anal. Calcd for $C_{28}H_{32}NO_5P$ C, 68.14; H, 6.54; N, 2.84; Found C, 68.31; H, 6.32; N, 2.75.

(±)-Diethyl 1-(4-(dimethylamino)phenyl)-3-oxo-3-phenylpropylphosphonate (3s) IR (KBr, cm^{-1}) 2934, 1733, 1690, 1523, 1257, 1027; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.12 (t, *J*~7.0 Hz, 3H), 1.28 (t, *J* ~7.0 Hz, 3H), 2.89 (s, 6 H), 3.60-3.76 (m, 3H), 3.90-3.95 (m, 2H), 4.04-4.09 (m, 2H), 6.66 (d, *J* = 8.0 Hz, 2H), 7.29-7.30 (m, 2H), 7.42-7.45 (m, 2H), 7.52-7.55 (m, 1H), 7.95 (d, *J* = 7.5 Hz, 2H); Some unassigned peaks at δ 2.98 (s) and 6.87-6.95 (m) also appeared in the spectrum; ^{13}C NMR (125 MHz, $CDCl_3$) δ 16.3 and 16.4 (d, *J* = 5.6 Hz), 37.9 (d, *J* = 140.6 Hz), 39.3, 40.5, 61.9 and 63.0 (d, *J* = 7.4 Hz each), 110.9, 112.6, 114.7, 120.0, 121.4, 123.2 (d, *J* = 6.8 Hz), 128.1, 128.6, 129.8 (d, *J* = 6.6 Hz), 133.1, 136.8, 145.9, 146.8, 149.8 (d, *J* = 1.4 Hz), 196.8 (d, *J* = 15.0 Hz); Other peaks at δ 55.9 and in the region of 110.0-150.0 corresponds to unassigned peaks in ^{1}H NMR; ^{31}P NMR (162 MHz, $CDCl_3$) δ 30.0 (s); LC/MS m/z 390 $[M + H]^+$.

(±)-Diethyl 2-benzoyl-1-(4-(dimethylamino)phenyl)-3-oxobutylphosphonate (3t) yield: 0.130g, (18%); light brown solid; mp 172-174 °C; IR (KBr, cm^{-1}) 1696, 1605, 1522, 1448, 1253, 1050, 965; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.99 and 1.05 (t, *J* = 7.1 Hz each, 6H), 1.87 (s, 3H), 2.95 (s, 6H), 3.60-3.63 (m, 1H), 3.65-3.82 (m, 3H), 4.29 (dd, *J* = 21.5 and 11.8 Hz, 1H), 5.51 (dd→t, *J* = 11.9 and 11.8 Hz, 1H), 6.69 (d, *J* = 9.0 Hz, 2H), 7.26- 7.28 (m, 2H), 7.51-7.54 (m, 2H), 7.60-7.64 (m, 1H), 8.17 (d, *J* = 9.5 Hz, 2H); Some unassigned peaks at δ 2.98 (s) and 6.87-6.95 (m) also appeared in the spectrum. ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.9 and 16.1 (d, *J* = 6.6 Hz), 27.1, 40.4, 43.3 (d, *J* = 138.1 Hz), 62.1 and 62.9 (d, *J* = 7.1 Hz), 63.6, 110.7, 112.6, 114.6, 120.1, 121.5, 128.7, 19.1, 130.7, 133.6, 136.8, 145.7, 146.6, 150.0, 193.6, 202.0 (d, *J* = 17.1 Hz), The peaks at δ 55.9 and extra peaks at the region of 110.0-150.0 correspond to the unassigned peas in ^{1}H NMR; ^{31}P NMR (162 MHz, $CDCl_3$) δ 25.6 (s); LC/MS m/z 432 $[M + H]^+$.

(xi) The reaction of phosphonate 1e with diketone 2b: **Synthesis of (±)-diethyl 2-acetyl-1-(4-(dimethylamino)phenyl)-3-oxobutyl)phosphonate (3u)** A method similar to the synthesis of **3k** was used using similar molar quantities**.** Yield 0.570 g, (89%); off-white solid; mp 198-200 °C; IR (KBr, cm^{-1}) 1698, 1609, 1517, 1357, 1236, 1160, 1050,; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.09 and 1.24 (two sets of triplet, *J* = 7.2 Hz each, 6H), 1.82 (s, 3H), 2.33 (s, 3H), 2.89 (s, 6H), 3.63-3.72 (m, 1H), 3.81-3.99 (m, 4H), 4.60 (dd→t, *J*~ 11.6 Hz each, 1H), 6.62 (d, *J* = 8.8 Hz, 2H), 7.09 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 16.2 and 16.3 (two sets of doublets, *J* = 5.5 Hz each), 28.1, 30.7, 40.5, 42.9 (d, *J* = 139.3 Hz), 62.4 and 63.2 (two sets of doublets, *J* = 7.1 Hz each), 69.6, 112.7, 120.1 (d, *J* = 7.8 Hz), 130.4 (d, *J* = 5.7 Hz), 149.9, 201.8, 202.1 (d, *J* = 18.1 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 26.0. LC/MS m/z 370 $[M + H]^+$; Anal. Calcd for $C_{18}H_{28}NO_5P$ C, 58.53; H, 7.64; N, 3.79. Found C, 58.31; H, 7.43; N, 3.88.

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Notes and references

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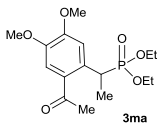
[$]The ^{31}P NMR spectrum for the crude reaction mixture obtained from the reaction of **1a** with **2c** showed the presence of compounds **3b** and **3d**.

†Along with **3m**, another type of compound **3ma** was also isolated in 1:1 ratio. The primary investigations on the spectral data of pure crystallized **3ma** (see experimental section for details) support the molecular structure as given below



3ma

Electronic Supplementary Information (ESI) available: [details of any supplementary information available should be included here]. See DOI: 10.1039/b000000x/

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12. Considering **3d,** using B3LYP/6-31G**, the difference in energy for optimised structures of **X** (-1033773.793 kcal/mol) and **Y** (-1033773.712 kcal/mol) is only 0.081 kcal/mol.