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Synthesis of a Series of γ-Keto Allyl Phosphonates†

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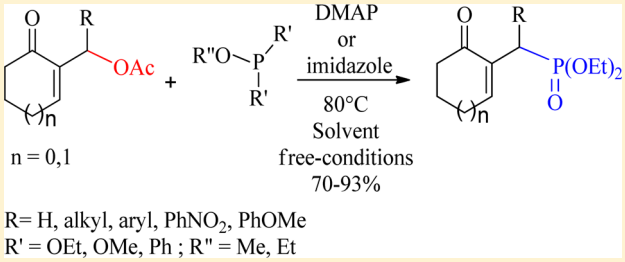
Supporting Information

ABSTRACT: Under solvent-free conditions and at 80 °C, a DMAP- or imidazole-mediated clean and rapid conversion of cyclic Morita−Baylis−Hillman (MBH) acetates into the corresponding γ-keto allyl phosphonates in 70−93% yields is described herein. This allylic nucleophilic substitution works well with primary and secondary acetates bearing, at the β′-position, linear or branched alkyl groups and aryl groups.



INTRODUCTION

Phosphonates are useful intermediates in organic synthesis[1] in addition to their various biological applications.[2] Usually, they are prepared in a three-step sequence, involving first the mesylation of the corresponding alcohols, then the conversion of the intermediate mesylates into their halides, and finally, these derivatives give the desired phosphonates through a Michaelis−Arbusov reaction.[3]

Over the past few decades, much effort has been spent to develop the short-step synthesis of phosphonates. Accordingly, Basavaiah and co-workers have reported the preparation of allylic phosphonates from the reaction of acyclic MBH acetates with triethyl phosphite.[4] Alternatively, the addition of various dialkyl phosphites to BH acetates in *N*,*O*-bis(trimethylsilyl)-acetamide afforded the phosphono-unsaturated esters.[5] Moreover, using either DABCO or triphenyl phosphine as a nucleophilic additive, the conversion of allyl bromides and chlorides in the presence of trialkyl phosphites into the corresponding allylic phosphonates has also been described.[6] The reaction of allyl bromides with diethylphosphite/NaH has also been reported as an alternative synthetic pathway to allyl phosphonates.[7] Recently, Wu and co-workers described the rearrangement of vinyl phosphonates into allyl phosphonates as useful intermediates in their synthetic route for the total synthesis of lycopene.[8] More interestingly, Wiemer and co-workers have recently described a ZnI_2-mediated direct conversion of allyl and benzyl alcohols into the corresponding phosphonates.[9]

In the course of our study on the development of the chemistry of MBH, we have studied the behavior of cyclic MBH adducts with a large variety of nucleophiles.[10] Recently, we reported the first DMAP-mediated, palladium-free Tsuji−Trost-type reaction of cyclic and acyclic MBH alcohols with active methylene compounds.[11] In contrast to acyclic phosphonates derived from MBH adducts that have been previously prepared by Basavaiah,[4] their cyclic homologues have not been previously described. In continuation of our study on the chemistry of allylic compounds, we wish to report a clean, rapid, and highly selective DMAP/imidazole-mediated palladium-free conversion of MBH acetates under solvent-free conditions into the corresponding allyl phosphonates in high yields.

RESULTS AND DISCUSSION

The starting material **1a** was prepared in a two-step sequence according to our previous reports.[10,11] In our first attempt, a mixture of allyl acetate **1a** (1 mmol) and triethylphosphite (1−3 mmol) was carried out in THF without any additive. After the reaction mixture was stirred at room temperature for 24 h, the starting materials were completely recovered. However, during reflux in THF, a sluggish reaction occurred. After 24 h, we observed that only ∼40% of the starting acetate **1a** was converted into the corresponding allylic phosphonate **2a** in 60% yield. Therefore, in order to improve the conversion percentage of the starting materials, we investigated this reaction at 80 °C under solvent-free conditions using DMAP as an additive (commonly used in our previous reports) to mediate nucleophilic allylic substitutions of MBH derivatives.[11] After optimizing the reaction conditions, we observed that a stoichiometric amount of DMAP (1 equiv) was required for a total conversion of acetate **1a** into the corresponding phosphonate **2a** (30 min, 92% yield) (Scheme 1, Table 1, entry 1).

In a previous study, Kim and co-workers[6] reported that, in the reaction of primary MBH bromides with triethyl phosphite, the DABCO behaved as a hard nucleophile that directly displaced the bromide ion via an S_N2 reaction, and then the

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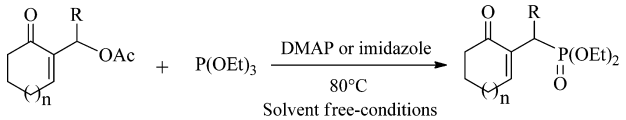
Scheme 1. Synthesis of γ-Keto Allyl Phosphonates 2



triethyl phosphite, as a soft nucleophile, reacted onto the resulting DABCO salt in a 1,4-addition/DABCO release, yielding the S_N2' phosphonates (Scheme 2, eq 1). In the present study, DMAP, known to be a soft nucleophile, first reacted in a 1,4-addition/elimination of the acetoxy moiety, affording the S_N2' DMAP salt, on which triehyl phosphite further reacted in a β'-1,4-addition/DMAP release, affording the S_N2' phosphonate (Scheme 2, eq 2). Therefore, the regioselectivity observed in the two protocols is different. Indeed, in the previous study, the overall allylic nucleophilic substitution on MBH derivatives afforded the S_N2'-type products; in the present work, it yields the S_N2-type products resulting from two successive S_N2'-type products.

Next, in order to investigate the scope and the limitations of this rapid and efficient synthetic method, we investigated the behavior of a variety of MBH acetates **1b−l** toward triethylphoshite or thoxydiphenylphosphine under the conditions listed above (solvent-free conditions, 80 °C). Our results showed that the nucleophilic allylic substitution worked well with six-membered cyclic MBH adducts **1b−g** using DMAP or imidazole (Table 1, entries 2−11) as well as with five-membered cyclic MBH **1h−l** using imidazole (Table 1, entries 12−16), which is usually employed as a powerful nucleophile to mediate various reactions of five-membered cyclic enones.[12] In all cases, we observed that the conversion of the primary acetates **1a** and **1h** and the secondary acetates **1b−g** and **1i−l** (R = linear/branched alkyl or aryl) occurred within 30−45 min, affording the corresponding allylic phosphonate or phosphine oxides **2a−p** in high to excellent yields (70−93%) (Scheme 1, Table 1).

CONCLUSIONS

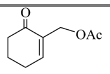
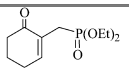
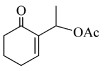
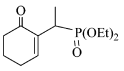
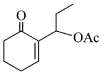
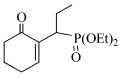
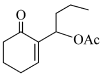
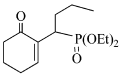
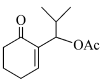
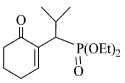
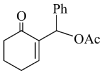
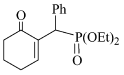
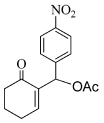
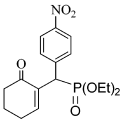
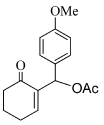
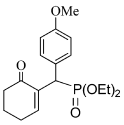
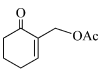
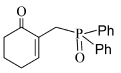
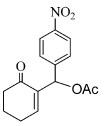
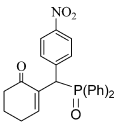
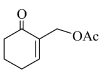
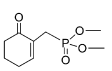
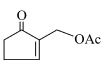
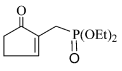
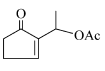
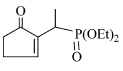
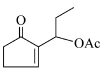
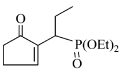
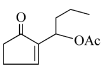
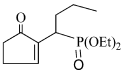
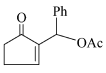
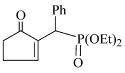
We have described an efficient protocol for the synthesis of a new series of γ-keto allyl phosphonates in good to excellent yields using MBH acetates as starting materials and either DMAP or imidazole as an additive. Mild reaction conditions, high regioselectivity, and solvent-free reactions are the attractive features of this synthetic methodology. We believe these γ-keto allyl phosphonates will be of much importance in organic synthesis and in medicinal chemistry.

EXPERIMENTAL SECTION

Materials and Methods. ^{1}H NMR and ^{13}C NMR spectra were recorded at 300 and 75 MHz, respectively, in $CDCl_3$, using TMS as an internal standard (chemical shifts in δ values, *J* in Hz). High-resolution mass spectra (HRMS) were recorded as TOF-HRMS on a micromass mass spectrometer. Mass spectra (EI) were recorded at 70 eV. Analytical thin-layer chromatography (TLC) was performed using silica gel 60 F254 precoated silica gel plates. Visualization was achieved by UV light (254 nm). Flash chromatography was performed using silicagel 60 and a gradient solvent system (dichloromethane/ether) as eluent.

General Procedure for the Preparation of Allyl Phosphonates ***2****.* A mixture of either DMAP or imidazole (1 equiv), $P(OEt)_3$ (1.2 equiv), and the allyl acetate **1** (1 equiv) was heated with stirring in an oil bath at 80 °C for the specified time (Table 1). The progress of the reaction was monitored by TLC using dichloromethane/ether. The mixture was neutralized with an aqueous solution of 4 M hydrochloric acid and extracted with CH_2Cl_2. The combined organic layers were

Table 1. DMAP- or Imidazole-Mediated Conversion of Acetates to Phosphonates

Entry		Acetate **1**	Additif	Reaction time/min		Phosphonate **2**	Yield (%)
1	**1a**		DMAP	30	**2a**		92
2	**1b**		DMAP	30	**2b**		82
3	**1c**		DMAP	30	**2c**		80
4	**1d**		DMAP	30	**2d**		83
5	**1e**		DMAP	30	**2e**		93
6	**1f**		Imidazole	45	**2f**		70
7	**1g**		Imidazole	45	**2g**		76
8	**1g**		Imidazole	45	**2h**		78
9	**1a**		DMAP	45	**2i**		84
10	**1g**		Imidazole	45	**2j**		78
11	**1a**		DMAP	30	**2k**		85
12	**1h**		Imidazole	30	**2l**		90
13	**1i**		Imidazole	40	**2m**		70
14	**1j**		Imidazole	40	**2n**		80
15	**1k**		Imidazole	40	**2o**		80
16	**1l**		Imidazole	40	**2p**		75

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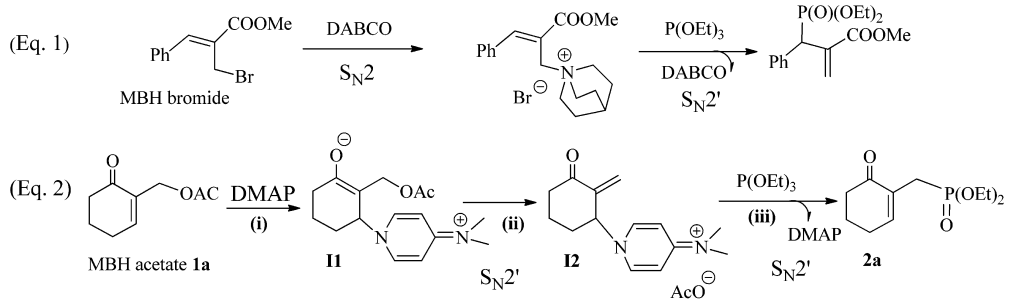
Scheme 2. Proposed Mechanisms for the Synthesis of Allyl Phosphonates from MBH Adducts



(iii): (a) 1,4-Addition
(b) DMAP elimination/Arbuzov rearrangement

neutralized with $NaHCO_3$ and washed with a saturated NaCl solution. They were further dried and concentrated. The residue was purified by column chromatography on silica gel (30% dichloromethane/ether) to give the pure allyl phosphonates **2** as yellow oils, with the exception of **2i** and **2j**, which were obtained as white solids.

*Diethyl ((6-Oxocyclohex-1-en-1-yl)methyl)phosphonate (**2a**).* Yield: 672 mg (92%), 2.97 mmol reaction scale. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.14 (t, J = 9.0 Hz, 6H), 1.87 (m, 2H), 2.32 (m, 4H), 2.75 (d, J_{P-H} = 21.0 Hz, 2H), 3.91 (q, J = 7.8 Hz, 2H), 3.93 (q, J = 7.2 Hz, 2H), 6.95 (t, J = 6.0 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 16.1, 16.2, 22.7, 24.7 (d, J_{C-P} = 140.36 Hz), 26.1, 37.8, 61.8, 61.9, 130.4 (d, J_{C-P} = 9 Hz), 149.0 (d, J_{C-P} = 9 Hz), 197.3 (d, J_{C-P} = 9 Hz). ^{31}P NMR (121 MHz, $CDCl_3$): δ 27.0. HRMS (ESI-TOF): [M^+] calcd for $C_{11}H_{19}O_4P$ 246.1021, found 246.1027. GC-MS (EI, 70 eV): m/z 246 (100, M^+), 218 (50) [MH − C_2H_5], 109 (50) [M − $C_4H_{10}O_3P^\bullet$], 137 (12) [$C_4H_{10}O_3P^\bullet$].

*Diethyl (1-(6-Oxocyclohex-1-en-1-yl)ethyl)phosphonate (**2b**).* Yield: 584 mg (82%), 2.74 mmol reaction scale. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.18 (t, J = 9.0 Hz, 3H), 1.22 (t, J = 9.0 Hz, 3H), 1.25 (d, J = 6.0 Hz, 3H), 1.93 (m, 2H), 2.39 (m, 4H), 3.49 (qd, J = 9.0 Hz, J_{P-H} = 22.0 Hz, 1H), 3.95 (q, J = 9.0 Hz, 2H), 4.02 (q, J = 9.0 Hz, 2H), 7.04 (t, J = 4.5 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.7 (d, J_{C-P} = 5.25 Hz), 16.2, 16.3, 22.5, 26.1, 27.1 (d, J_{C-P} = 144 Hz), 37.9, 61.8, 61.9, 136.8 (d, J_{C-P} = 6 Hz), 147.4 (d, J_{C-P} = 8.2 Hz), 196.9 (d, J_{C-P} = 6 Hz). ^{31}P NMR (121 MHz, $CDCl_3$): δ 30.0. HRMS (ESI-TOF): [M^+] calcd for $C_{12}H_{21}O_4P$ 260.1177, found 260.1175. GC-MS (EI, 70 eV): m/z 260 (100, M^+), 231 (30) [M − C_2H_5], 123 (90) [M − $C_4H_{10}O_3P^\bullet$], 138 (12) [$C_4H_{10}O_3PH$].

*Diethyl (1-(6-Oxocyclohex-1-en-1-yl)propyl)phosphonate (**2c**).* Yield: 558 mg (80%), 2.55 mmol reaction scale. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.79 (t, J = 9.0 Hz, 3H), 1.16 (t, J = 9.0 Hz, 3H), 1.22 (t, J = 6.0 Hz, 3H), 1.55 (m, 2H), 1.94 (m, 2H), 2.39 (m, 4H), 3.36 (ddd, J = 3.0 Hz,10.5 Hz, J_{P-H} = 23.1 Hz, 1H), 3.92 (q, J = 6.0 Hz, 2H), 3.98 (q, J = 6.0 Hz, 2H), 7.05 (t, J = 6.0 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 12.5 (d, J_{C-P} = 15.3 Hz), 14.0, 16.3, 16.4, 22.8, 26.3 (d, J_{C-P} = 2.5 Hz), 29.4, 36.5 (d, J = 138.5 Hz), 61.7, 61.9, 135.0 (d, J_{C-P} = 6 Hz), 147.6 (d, J_{C-P} = 7.5 Hz), 197.7 (d, J_{C-P} = 6 Hz). ^{31}P NMR (121 MHz, $CDCl_3$): δ 29.6. HRMS (ESI-TOF): [M^+] calcd for $C_{13}H_{23}O_4P$ 274.1334, found 274.1354. GC-MS (EI, 70 eV): m/z 274 (55, M^+), 246 (25) [MH − C_2H_5], 137 (96) [M − $C_4H_{10}O_3P^\bullet$], 137 (90) [$C_4H_{10}O_3P^\bullet$].

*Diethyl (1-(6-Oxocyclohex-1-en-1-yl)butyl)phosphonate (**2d**).* Yield: 568 mg (83%), 2.38 mmol reaction scale. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.86 (t, J = 6.0 Hz, 3H), 1.24 (t, J = 3.0 Hz, 6H), 1.29 (m, 2H), 1.73 (m, 2H), 2.01 (m, 2H), 2.46 (m, 4H), 3.52 (ddd, J = 4.5, 11.1 Hz, J_{P-H} = 22.8 Hz, 1H), 3.92 (q, J = 6.0 Hz, 2H), 3.98 (q, J = 6.0 Hz, 2H), 7.11 (t, J = 6.0 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.6, 16.0, 16.3, 20.5, 22.7, 26.2, 29.4 (d, J_{C-P} = 24.75 Hz), 31.6 (d, J_{C-P} = 87 Hz), 38.0, 61.7, 61.8, 135.0 (d, J_{C-P} = 6.7 Hz), 147.6, (d, J_{C-P} = 7.5 Hz), 197.7 (d, J_{C-P} = 6 Hz). ^{31}P NMR (121 MHz, $CDCl_3$): δ 29.8. HRMS (ESI-TOF): [M^+] calcd for $C_{14}H_{25}O_4P$ 288.1490, found 288.1485. GC-MS (EI, 70 eV): m/z 288 (40, M^+), 259 (89) [M − C_2H_5], 151 (90) [M − $C_4H_{10}O_3P^\bullet$], 137 (6) [$C_4H_{10}O_3P^\bullet$].

*Diethyl (2-Methyl-1-(6-oxocyclohex-1-en-1-yl)propyl)-phosphonate (**2e**).* Yield: 637 (93%), 2.38 mmol reaction scale. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.88 (d, J = 6.0 Hz, 3H), 1.05 (d, J = 6.0 Hz, 3H), 1.23 (t, J = 9.0 Hz, 3H), 1.30 (t, J = 9.0 Hz, 3H), 2.02 (m, 2H), 2.16 (m, 1H), 2.48 (m, 4H), 3.38 (dd, J = 6.0 Hz, J_{P-H} = 22.5 Hz, 1H), 3.95 (q, J = 6.0 Hz, 2H), 4.08 (q, J = 6.0 Hz, 2H), 7.21 (t, J = 6.0 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 16.3, 16.4, 20.6 (d, J_{C-P} = 12 Hz), 22.1 (d, J_{C-P} = 7.5 Hz), 22.8, 26.3, 29.6 (d, J_{C-P} = 1.5 Hz), 38.0, 39.0 (d, J_{C-P} = 51.7 Hz), 61.4, 61.9, 134.9 (d, J_{C-P} = 5.2 Hz), 148.3 (d, J_{C-P} = 7.5 Hz), 197.6 (d, J_{C-P} = 7.5 Hz). ^{31}P NMR (121 MHz, $CDCl_3$): δ 29.8. HRMS (ESI-TOF): [M^+] calcd for $C_{14}H_{25}O_4P$ 288.1490, found 288.1506. GC-MS (EI, 70 eV): m/z 288 (10, M^+), 245 (8) [MH − (C_2H_5, CH_3)], 151 (100) [M − $C_4H_{10}O_3P^\bullet$], 137 (8) [$C_4H_{10}O_3P^\bullet$].

*(Diethyl ((6-Oxocyclohex-1-en-1-yl)(phenyl)methyl)phosphonate (**2f**).* Yield: 459 mg (70%), 2.04 mmol reaction scale. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.26 (t, J = 9.0 Hz, 3H), 1.36 (t, J = 9.0 Hz, 3H), 1.98 (m, 2H), 2.45 (m, 4H), 4.03 (q, J = 6.0 Hz, 2H), 4.08 (q, J = 6.0 Hz, 2H), 4.80 (d, J_{P-H} = 24.0 Hz, 1H), 7.22−7.48 (m, 5H), 7.66 (t, J = 3.0 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 16.1, 16.3, 25.2, 26.3, 38.1, 39.6 (d, J_{C-P} = 66.7 Hz), 62.2, 62.7, 125.5−129.6 (aromatics), 136.0 (d, J_{C-P} = 3 Hz), 149,0 (d, J_{C-P} = 6.7 Hz), 196.9 (d, J_{C-P} = 9.7 Hz). ^{31}P NMR (121 MHz, $CDCl_3$): δ 25.6. HRMS (ESI-TOF): [M^+] calcd for $C_{17}H_{23}O_4P$ 322.1334, found 322.1328. GC-MS (EI, 70 eV): m/z 322 (100, M^+), 293 (20) [M − C_2H_5], 184 (90) [MH − $C_4H_{10}O_3P^\bullet$], 138 (32) [$C_4H_{10}O_3PH$].

*Diethyl ((4-Nitrophenyl)(6-oxocyclohex-1-en-1-yl)methyl)-phosphonate (**2g**).* Yield: 482 mg (76%), 1.73 mmol reaction scale. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.29 (t, J = 6.0 Hz, 3H), 1.37 (t, J = 6.0 Hz, 3H), 2.03 (m, 2H), 2.51 (m, 4H), 4.11 (q, J = 6.0 Hz, 2H), 4.14 (q, J = 6.0 Hz, 2H), 4.91 (d, J_{P-H} = 24.0 Hz, 1H), 7.65−8.16 (AB, J = 9.0 Hz, 4H), 7.72 (t, J = 3.0 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 16.1, 16.2, 22.5, 26.4, 38.0, 40.8 (d, J_{C-P} = 141 Hz), 61.8, 62.8, 123.5−143.9 (aromatics), 147.0 (d, J_{C-P} = 3 Hz), 149.6 (d, J_{C-P} = 6.7 Hz), 196.7 (d, J_{C-} = 9.7 Hz). ^{31}P NMR (121 MHz, $CDCl_3$): δ 23.8. HRMS (ESI-TOF): [M^+] calcd for $C_{17}H_{22}NO_6P$ 367.1185, found 367.1191.

*Diethyl ((4-Methoxyphenyl)(6-oxocyclohex-1-en-1-yl)methyl)-phosphonate (**2h**).* Yield: 499 mg (78%), 1.82 mmol reaction scale. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.17 (t, J = 6.0 Hz, 3H), 1.28 (t, J = 6.0 Hz, 3H), 1.90 (m, 2H), 2.37 (m, 4H), 3.96 (q, J = 6.0 Hz, 2H), 4.04 (q, J = 6.0 Hz, 2H), 4.68 (d, J_{P-H} = 24.0 Hz, 1H), 7.28−7.32 (AB, J = 9.0 Hz, 4H), 7.56 (t, J = 3.0 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 16.2, 16.3, 22.5, 26.2, 38.0 (d, J_{C-P} = 141.6 Hz), 55.1, 62.7, 62.8, 113.7−135.8 (aromatics), 148.6 (d, J_{C-P} = 6.6 Hz), 158.6, 196.8 (d, J_{C-P} = 9.6 Hz). ^{31}P NMR (121 MHz, $CDCl_3$): δ 25.9. HRMS (ESI-TOF): [M + H]$^+$ calcd for $C_{18}H_{26}O_5P$ 353.1512, found 353.1514.

*2-((Diphenylphosphoryl)methyl)cyclohex-2-enone (**2i**).* Yield: 773 mg (84%), mp 106−107 °C, 2.97 mmol reaction scale. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.79 (m, 2H), 2.22 (t, J = 6.0 Hz, 2H), 2.31 (m, 2H), 3.37 (d, J_{P-H} = 12.0 Hz, 2H), 7.31 (t, J = 6.0 Hz, 1H), 7.44−7.77 (m, 10H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 22.6, 26.2, 27.8 (d, J = 68.8 Hz), 37.6, 128.2−131.6 (aromatics), 133.1 (d, J_{C-P} = 3

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Hz), 150.2 (d, J_{C-P} = 7.5 Hz), 197.2 (d, J_{C-P} = 4.5 Hz). ^{31}P NMR (121 MHz, $CDCl_3$): δ 30.4. HRMS (ESI-TOF): $[M + H]^+$ calcd for $C_{19}H_{20}O_2P$ 311.1195, found 311.1206.

*2-((Diphenylphosphoryl)(4-nitrophenyl)methyl)cyclohex-2-enone (**2j**).* Yield: 581 mg (78%), mp 214−215 °C, 1.73 mmol reaction scale. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.74 (m, 2H), 2.27 (m, 4H), 5.42 (d, J_{P-H} = 6.0 Hz, 1H), 7.96 (t, J = 6.0 Hz, 1H), 7.30−8.04 (m, 14H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 22.3, 26.4, 37.7, 41.3 (d, J_{C-P} = 66 Hz), 123.7−135.3 (aromatics), 143.9 (d, J_{C-P} = 4.5 Hz), 151.3 (d, J_{C-P} = 6 Hz), 196.4 (d, J_{C-P} = 6 Hz). ^{31}P NMR (121 MHz, $CDCl_3$): δ 31.7. HRMS (ESI-TOF): $[M^+]$ calcd for $C_{25}H_{23}NO_4P$ 431.1286, found 431.1288.

*Dimethyl ((6-Oxocyclohex-1-en-1-yl)methyl)phosphonate (**2k**).* Yield: 550 mg (85%), 2.97 mmol reaction scale. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.03 (m, 2H), 2.47 (m, 4H), 2.84 (d, J_{P-H} = 21.0 Hz, 2H), 3.70 (s, 3H), 3.74 (s, 3H), 7.02 (t, J = 6.0 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 22.6, 23.8 (d, J_{C-P} = 139.8 Hz), 26.1, 37.7, 52.4, 52.5, 130.1 (d, J_{C-P} = 9.5 Hz), 149.2 (d, J_{C-P} = 8.8 Hz), 197.2 (d, J_{C-P} = 4.7 Hz). ^{31}P NMR (121 MHz, $CDCl_3$): δ 27.0. HRMS (ESI-TOF): $[M + H]^+$ calcd for $C_9H_{16}O_4P$ 219.0781, found 219.0788.

*Diethyl ((5-Oxocyclopent-1-en-1-yl)methyl)phosphonate (**2l**).* Yield: 676 mg (90%), 3.24 mmol reaction scale. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.30 (t, J = 9.0 Hz, 6H), 2.43 (m, 2H), 2.66 (t, J = 3.0 Hz, 2H), 2.76 (d, J_{P-H} = 21.0, 2H), 4.11 (q, J = 9.0 Hz, 2H), 4.14 (q, J = 9.0 Hz, 2H), 7.72 (t, J = 4.5 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 16.3, 16.4, 21.4 (d, J_{C-P} = 140.2 Hz), 26.8, 33.7, 62.1, 62.2, 136.5 (d, J_{C-P} = 7.5 Hz), 161.1 (d, J_{C-P} = 7.5 Hz), 207.9 (d, J_{C-P} = 6 Hz). ^{31}P NMR (121 MHz, $CDCl_3$): δ 25.8. HRMS (ESI-TOF): $[M + H]^+$ calcd for $C_{10}H_{18}O_4P$ 233.0937, found 233.0948. GC-MS (EI, 70 eV): m/z 232 (100, M^+), 204 (40) $[MH - C_2H_5]$, 217 (10) $[M - CH_3]$, 187 (30) $[M - C_2H_5]$, 95 (88) $[MH - C_4H_{10}O_3P^\bullet]$, 137 (4) $[C_4H_{10}O_3P^\bullet]$.

*Diethyl (1-(5-Oxocyclopent-1-en-1-yl)ethyl)phosphonate (**2m**).* Yield: 511 mg (70%), 2.97 mmol reaction scale. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.26 (t, J = 6.0 Hz, 3H), 1.32 (t, J = 6.0 Hz, 3H), 1.39 (d, J = 6.0 Hz, 3H), 2.43 (t, J = 6.0 Hz, 2H), 2.64 (m, 2H), 3.12 (qd, J = 6.0 Hz, J_{P-H} = 24.0 Hz, 1H), 4.03 (q, J = 6.0 Hz, 2H), 4.11 (q, J = 6.0 Hz, 2H), 7.68 (t, J = 3.0 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.6, 16.3, 16.4, 26.7, 26.8 (d, J_{C-P} = 74 Hz), 34.0, 62.1, 62.2, 143.4 (d, J_{C-P} = 6.75 Hz), 159.9 (d, J_{C-P} = 7.5 Hz), 207.6 (d, J_{C-P} = 6 Hz). ^{31}P NMR (121 MHz, $CDCl_3$): δ 25.8. HRMS (ESI-TOF): $[M + H]^+$ calcd for $C_{11}H_{20}O_4P$ 247.1094, found 247.1095. GC-MS (EI, 70 eV): m/z 246 (100), 231 (50) $[M - CH_3]$, 218 (20) $[MH - C_2H_5]$, 109 (100) $[M - C_4H_{10}O_3P^\bullet]$, 138 (44) $[C_4H_{10}O_3PH]$.

*Diethyl (1-(5-Oxocyclopent-1-en-1-yl)propyl)phosphonate (**2n**).* Yield: 569 mg (80%), 2.74 mmol reaction scale. ^{1}H NMR (300 MHz, CD_2Cl_2): δ 0.77 (t, J = 6.0 Hz, 3H), 1.14 (t, J = 6.0 Hz, 3H), 1.19 (t, J = 6.0 Hz, 3H), 1.74 (m, 2H), 2.32 (t, J = 6.0 Hz, 2H), 2.57 (m, 2H), 2.85 (ddd, J = 6.0, 15.0 Hz, J_{P-H} = 21.7 Hz, 1H), 3.90 (q, J = 6.0 Hz, 2H), 3.96 (q, J = 6.0 Hz, 2H), 7.55 (t, J = 3.0 Hz, 1H). ^{13}C NMR (75 MHz, CD_2Cl_2): δ 13.8 (d, J_{C-P} = 15 Hz), 18.0, 18.1, 24.6 (d, J_{C-P} = 9.75 Hz), 28.6, 35.7, 35.8 (d, J_{C-P} = 138.7 Hz), 63.8, 63.9, 143.3 (d, J_{C-P} = 7.5 Hz), 162.0 (d, J_{C-P} = 7.5 Hz), 209.7 (d, J_{C-P} = 6 Hz). ^{31}P NMR (121 MHz, $CDCl_3$): δ 30.6. HRMS (ESI-TOF): $[M + H]^+$ calcd for $C_{12}H_{22}O_4P$ 261.1250, found 261.1263. GC-MS (EI, 70 eV): m/z 260 (100, M^+), 215 (20) $[M - C_2H_5O_2]$, 123 (100) $[M - C_4H_{10}O_3P^\bullet]$, 138 (52) $[C_4H_{10}O_3PH]$.

*Diethyl (1-(5-Oxocyclopent-1-en-1-yl)butyl)phosphonate (**2o**).* Yield: 558 mg (80%), 2.55 mmol reaction scale. ^{1}H NMR (300 MHz, CD_2Cl_2): δ 0.87 (t, J = 9 Hz, 3H), 1.25 (t, J = 6.0 Hz, 6H), 1.30 (m, 2H), 1.81 (m, 2H), 2.44 (t, J = 6.0 Hz, 2H), 2.66 (m, 2H), 3.08 (ddd, J = 3.0, 12.0 Hz, J_{P-H} = 21.7 Hz, 1H), 4.01 (q, J = 6.0 Hz, 2H), 4.07 (q, J = 6.0 Hz, 2H), 7.66 (t, J = 3.0 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.6, 16.2, 16.3, 20.6 (d, J_{C-P} = 13.5 Hz), 26.7, 30.9 (d, J_{C-P} = 4.5 Hz), 31.5 (d, J_{C-P} = 189.7 Hz), 33.8, 62.0, 62.1, 141.9 (d, J_{C-P} = 7.5 Hz), 160.1 (d, J_{C-P} = 6.7 Hz), 207.9 (d, J_{C-P} = 6 Hz). ^{31}P NMR (121 MHz, $CDCl_3$): δ 30.8. HRMS (ESI-TOF): $[M + H]^+$ calcd for $C_{13}H_{24}O_4P$ 275.1407, found 275.1118. GC-MS (EI, 70 eV): m/z 274 (50, M^+), 259 (8) $[M - CH_3]$, 245 (92) $[M - C_2H_5]$, 232 (30) $[MH - C_3H_7]$, 137 (94) $[M - C_4H_{10}O_3P^\bullet]$, 138 (49) $[C_4H_{10}O_3PH]$.

*Diethyl ((5-Oxocyclopent-1-en-1-yl)(phenyl)methyl)phosphonate (**2p**).* Yield: 501 mg (75%), 2.17 mmol reaction scale. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.98 (t, J = 6.0 Hz, 3H), 1.18 (t, J = 6.0 Hz, 3H), 2.31 (t, J = 6.0 Hz, 2H), 2.58 (m, 2H), 3.82 (q, J = 6.0 Hz, 2H), 3.94 (q, J = 6.0 Hz, 2H), 4.27 (d, J_{P-H} = 24.0 Hz, 1H), 7.17−7.38 (m, 5H), 8.03 (t, J = 3 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 16.2, 16.4, 26.8, 33.5, 39.4 (d, J_{C-P} = 139.5 Hz), 62.4, 63.0, 127.3−134.8 (aromatics), 141.3 (d, J_{C-P} = 5.25 Hz), 160.8 (d, J_{C-P} = 6 Hz), 207.3 (d, J_{C-P} = 9.7 Hz). ^{31}P NMR (121 MHz, $CDCl_3$): δ 27.7. HRMS (ESI-TOF): $[M + H]^+$ calcd for $C_{16}H_{22}O_4P$ 309.1250, found 309.1254. GC-MS (EI, 70 eV): m/z 308 (100, M^+), 279 (10) $[M - C_2H_5]$, 234 (18) $[M - C_5H_{14}O]$, 171 (48) $[M - C_4H_{10}O_3P^\bullet]$, 138 (2) $[C_4H_{10}O_3PH]$.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b02106.

Spectral data for compounds **2a**−**p** (PDF)

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Notes

The authors declare no competing financial interest.

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■ DEDICATION

†Dedicated to Professors M. M. El Gaied and A. Baklouti on the occasion of their 70th birthdays.

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