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Synthesis of Cyclopentenones via Intramolecular HWE and the Palladium-Catalyzed Reactions of Allylic Hydroxy Phosphonate Derivatives

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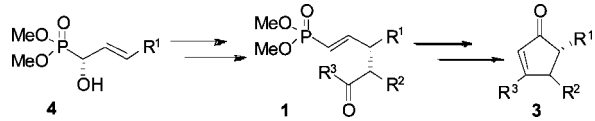


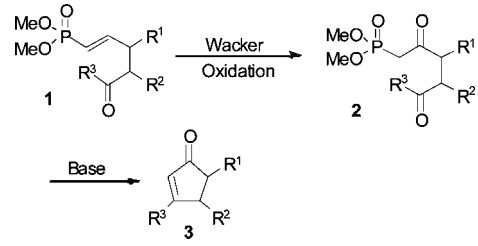
Palladium-catalyzed decarboxylative rearrangement of nonracemic phosphono allylic acetoacetates, or the intermolecular allylic substitution of nonracemic phosphono allylic carbonates with *tert*-butyl acetoacetate followed by hydrolysis and decarboxylation, gave ω-ketovinyl phosphonates. A highly regioselective Wacker oxidation gave the ω,β-diketophosphonates which underwent intramolecular HWE reaction to give nonracemic cyclopentenones. An aldol condensation leading to phosphonocyclopentenones was competitive with the HWE reaction. The stereochemistry of the cyclopentenone and the ratio of HWE to aldol products were dependent upon the choice of base used in the reaction.

Introduction

The cyclopentenone ring system is a structural feature found in numerous natural products.[1] Consequently, methods for the synthesis of the cyclopentenone ring system, particularly with control of absolute stereochemistry, are highly desirable.[2] An attractive method for generating cyclopentenones is the intramolecular Horner−Wadsworth−Emmons (HWE) reaction (Scheme 1),[3] which has seen application in natural product synthesis, for example Jasmone,[3a] Jatraphone,[3b] modhephene,[3c] and carbacephalosporins.[3d]

The formation of cyclopentenones **3** via the intramolecular HWE reaction requires access to the precursor diketophosphonates **2**. Among the published methods for forming diketo phosphonates **2**, the Wacker oxidation of the vinyl phosphonates **1** caught our attention.[4] In this remarkable reaction, a vinyl phosphonate **1** is oxidized with high regioselectivity to give a β-ketophosphonate **2**.

SCHEME 1. Formation of Cyclopentenones via the Intramolecular HWE Reaction



As part of an ongoing program[5] exploring the chemistry of allylic hydroxy phosphonates **4** and following the original work of Zhu and Lu,[6] we had shown that substituted vinyl phospho-

(1) For examples of cyclopenentone-containing natural products see: (a) Roberts, S. M.; Santoro, M. G.; Sickle, E. S. *J. Chem. Soc., Perkin Trans. 1* **2002**, 1735. (b) Howe, G. A. *Proc. Natl. Acad. Sci. U.S.A.* **2001**, *98*, 12317.

(2) For examples of cyclopentenone synthesis see: (a) Piancatelli, G.; D'Auria, M.; D'Onofrio, F. *Synthesis* **1994**, 867, and references cited therein. (b) Schore, N. E. *Org. React.* **1991**, *40*, 1. (c) Pauson, P. L. *Tetrahedron* **1985**, *41*, 5855. (d) Llebaria, A.; Moretó, J. M. *J. Organomet. Chem.* **1993**, *451*, 1. (e) Piancatelli, G. *Heterocycles* **1982**, *19*, 1735. (f) Ellison, R. A. *Synthesis* **1973**, 397.

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(5) (a) De la Cruz, M. A.; Shabany, H.; Spilling, C. D. *Phosphorus, Sulfur Silicon* **1999**, *144−146*, 181. (b) Shabany, H.; Spilling, C. D. *Tetrahedron Lett.* **1998**, *39*, 1465. (c) Thanavaro, A.; Spilling, C. D. *Phosphorus, Sulfur Silicon* **2002**, *177*, 1583. (d) Boehlow, T. R.; Spilling, C. D. *Tetrahedron Lett.* **1996**, *37*, 2717.

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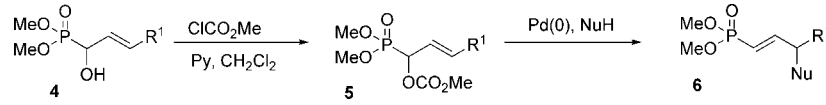
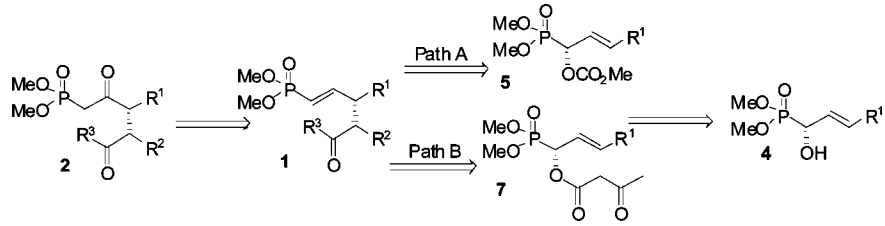
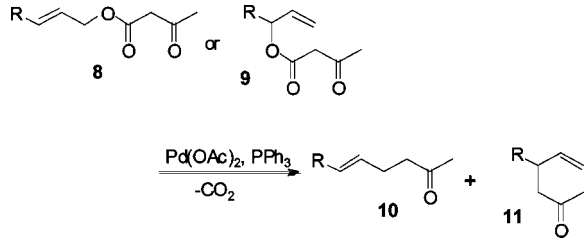
SCHEME 2. Palladium-Catalyzed Nucleophilic Substitution Reaction of Phosphono Allylic Carbonates



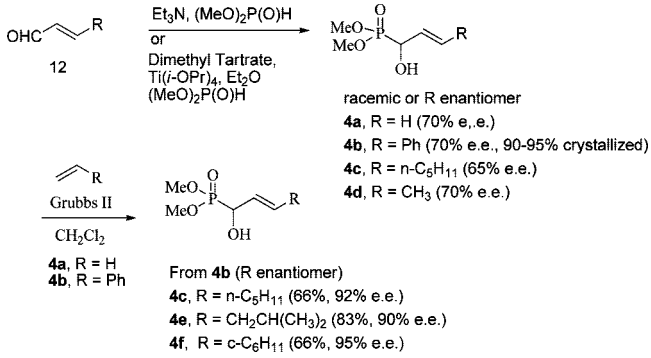
SCHEME 3. Proposed Methods for the Asymmetric Synthesis of Diketophosphonates



SCHEME 4. The Palladium-Catalyzed Carroll Rearrangement



SCHEME 5. Preparation of Allylic Hydroxy Phosphonates



nates **6** could be formed by the palladium-catalyzed nucleophilic substitution reactions of the carbonate derivatives **5** of allylic hydroxy phosphonates **4** (Scheme 2).[7,8] Addition of the nucleophile takes place exclusively at the 3-position to give the γ-substituted vinyl phosphonates **6** in high yield and studies with nonracemic allylic hydroxy phosphonate derivatives demonstrate that the reaction proceeds with complete chirality transfer.[8] Furthermore, continued research has led to methods for forming hydroxy phosphonates with high enantiopurity.[9] In particular, the metal-catalyzed asymmetric phosphonylation of aldehydes[10] and enzymatic kinetic resolution[11] provides efficient methods for asymmetric synthesis of allylic hydroxy phosphonates.

It was hypothesized that using the exquisite control of regio- and stereochemistry afforded by the phosphonate moiety, it should be possible to construct nonracemic diketophosphonate substrates for the intramolecuar HWE reaction and therefore develop a route to nonracemic cyclopentenones (Scheme 3). In particular, two pathways can be envisioned that would allow the stereospecific introduction of a ketone via C−C bond formation, for example, palladium-catalyzed intermolecular nucleophilic substitution (path A) or palladium-catalyzed intramolecular rearrangement of acetoacetoxy phosphonates (path B). Clearly, other well-known reactions of allylic alcohols, such as the variants of the Claisen rearrangement,[12] could also prove fruitful.

The Carroll rearrangement,[13] which was first reported in the 1940s, is the thermal 3,3 sigmatropic rearrangement of allylic acetoacetate esters to β-keto acids followed by decarboxylation to afford γ,δ-unsaturated ketones. However, since the reaction requires a high temperature (usually higher than 180 °C) and is sensitive to the structure of the substrate, it has not been widely used in organic synthesis.[14] In 1980, Tsuji and co-workers reported the palladium-catalyzed Carroll rearrangement (Scheme 4).[15] The rearrangement of allylic esters **8** or **9** in the presence of $Pd(OAc)_2$ and phosphine ligands in refluxing THF proceeded smoothly to give a regioisomeric mixture of γ,δ-unsaturated methyl ketones **10** and **11**. There have been several recent reports of methods to control both the regio- and enantioselec-

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(9) For recent reviews see: (a) Kolodiazhnyi, O. I. *Tetrahedron: Asymmetry* **2005**, *16*, 3295. (b) Wiemer, D. F. *Tetrahedron* **1997**, *53*, 16609. (c) Davies, S. R.; Mitchell, M. C.; Cain, C. P.; Devitt, P. G.; Taylor, R. J.; Kee, T. P. *J. Organomet. Chem.* **1998**, *550*, 29.

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(13) (a) Carroll, M. F. *J. Chem. Soc.* **1940**, 704. (b) Carroll, M. F. *J. Chem. Soc.* **1940**, 1266. (c) Carroll, M. F. *J. Chem. Soc.* **1941**, 507. (d) Kimel, W.; Cope, A. C. *J. Am. Chem. Soc.* **1943**, *65*, 1992.

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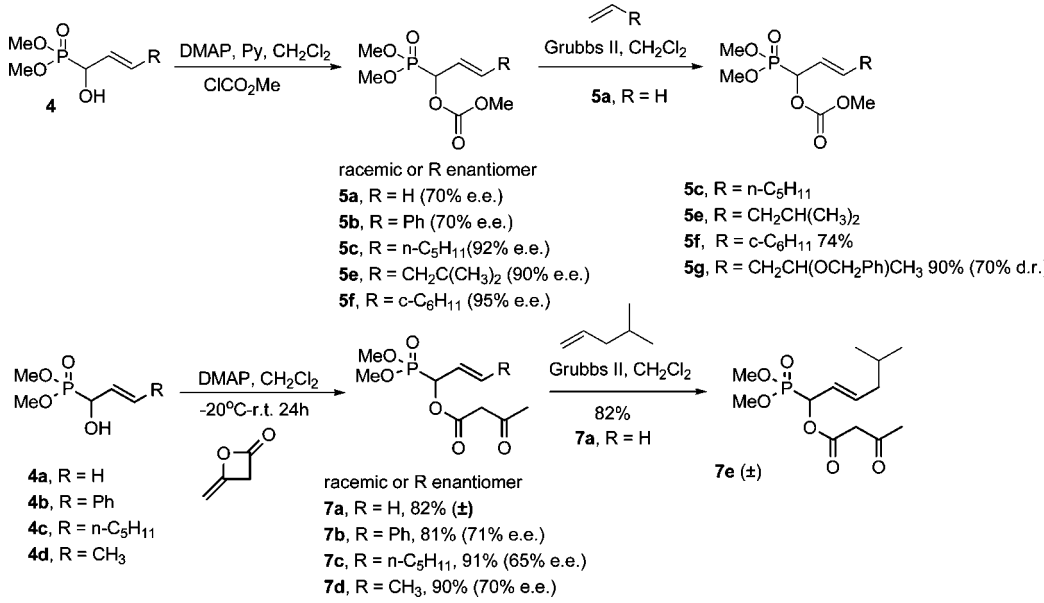
(15) (a) Tsuji, J.; Yamada, T.; Minami, I.; Yuhara, M.; Nisar, M.; Shimizu, I. *J. Org. Chem.* **1987**, *52*, 2988. (b) Shimizu, I.; Yamada, T.; Tsuji, J. *Tetrahedron Lett.* **1980**, *21*, 3199. (c) Tsuji, J. *Pure Appl. Chem.* **1982**, *54*, 197, and references cited therein.

SCHEME 6. Preparation of the Acetoacetate and Methylcarbonate Derivatives of Hydroxy Allylic Phosphonates



tivity of the Carroll rearrangement through the choice of metal complex employed as the catalyst.[16]

Results

By using previously published reaction procedures, the racemic hydroxy phosphonates **4a**−**d** were prepared (Scheme 5) by the Et_3N-catalyzed addition of dimethyl phosphite to the corresponding aldehyde **12**.[17] The nonracemic (*R*) phosphonates **4a**−**d** (∼70% ee) were prepared by catalytic asymmetric phosphonylation, using (L)-dimethyl tartrate and titanium isopropoxide as catalysts.[10a] Alternatively, the hydroxy phosphonates could be prepared by the cross-metathesis reaction of phosphonates **4a** or **4b** with a terminal alkene.[18] In particular, the phosphonates with high enantiomeric excess (**4c**−**f**) were prepared from the cross-metathesis between the cinnamyl hydroxy phosphonate **4b** and the corresponding alkenes. The hydroxy phosphonate **4b** can be crystallized to high enantiomeric purity (90−95% ee).

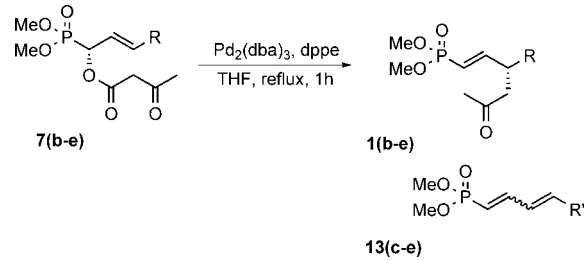
The phosphono allylic carbonates **5** were prepared either from corresponding hydroxy phosphonate **4** by reaction with methyl chloroformate and pyridine in CH_2Cl_2 (Scheme 6) or by cross-metathesis between the acrolein phosphono carbonate **5a** and a terminal alkene (Scheme 6) as previously described.[18] Alternatively, reaction of hydroxy phosphonates **4** with diketene in the presence of a catalytic amount of DMAP yielded the phosphono acetoacetates **7** in 81−91% yields (Scheme 6). The phosphono acetoacetates **7** were not stable and decomposed to starting material if stored for prolonged periods of time. The phosphono acetoacetates **7** could also be prepared by cross-metathesis.[18] Reaction of **7a** with 4-methyl-1-pentene and Grubbs second generation catalyst in CH_2Cl_2 gave phosphono acetoacetate **7e**.

(16) (a) Tunge, J. A.; Burger, E. C. *Eur. J. Chem.* **2005**, 1715. (b) Burger, E. C.; Tunge, J. A. *Org. Lett.* **2004**, *6*, 4113. (c) Burger, E. C.; Tunge, J. A. *Chem. Commun.* **2005**, 2835. (d) He, H.; Zheng, X.-J.; Dai, L.-X.; You, S.-L. *Org. Lett.* **2007**, *9*, 4339.

(17) (a) Baraldi, P. G.; Guarneri, M.; Moroder, F.; Pollini, G. P.; Simoni, D. *Synthesis* **1982**, 653. (b) Texier-Boullet, F.; Foucaud, A. *Synthesis* **1982**, 165.

(18) He, A.; Yan, B.; Thanavaro, A.; Spilling, C. D.; Rath, N. P. *J. Org. Chem.* **2004**, *69*, 8643.

TABLE 1. The Palladium-Catalyzed Decarboxylative Rearrangement of Phosphono Allylic Acetoacetates



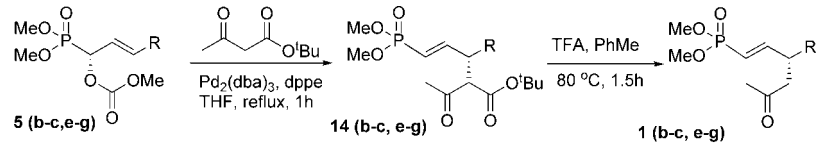
entry	compd	R	% ee (**4**)	% yield **1** (% ee)[a]	% yield **13**[b]
1	**b**	Ph	71	56 (71)	
2	**c**	n-C_5H_{11}	65	61 (65)	27
3	**d**	CH_3	70	71 (70)	2
4	**e**	$CH_2CH(CH_3)_2$	(±)	35 (±)	31

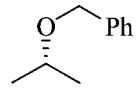
[a] Isolated yield; [b] Conversion measured by ^{31}P NMR spectroscopy

Palladium-catalyzed intramolecular decarboxylative rearrangement [$Pd_2(dba)_3$, dppe] of the phosphono acetoacetates **7** gave the vinyl phosphonates **3** (Table 1). However, with the exception of **7b**, which does not possess a δH, the competitive formation of diene **13** as a mixture of geometric isomers was observed. In each of the examples studied, the enantiomeric ratio of the vinyl phosphonate product **1** reflected the enantiomeric ratio of the starting hydroxy phosphonate **4**, demonstrating the stereospecific nature of the reaction. Attempts to improve the yield of vinyl phosphonate **3** relative to the diene **13** by changes in solvent, ligand, or adding base were not successful. Attempted thermal rearrangement resulted in a multitude of products.

Treatment of phosphono allylic carbonates **5** with *tert*-butyl acetoacetate, $Pd_2(dba)_3$, and dppe in refluxing THF provided the vinyl phosphonates **14** as intermediates, which were taken directly into the next reaction without purification. After removing THF in vacuo, the reaction mixture was dissolved in toluene and TFA and heated at 80 °C for 1 h to afford the vinyl phosphonates **1** in good to high chemical yields (Table 2). The enantiomeric ratio of the vinyl phosphonates **1b**−**f**, determined

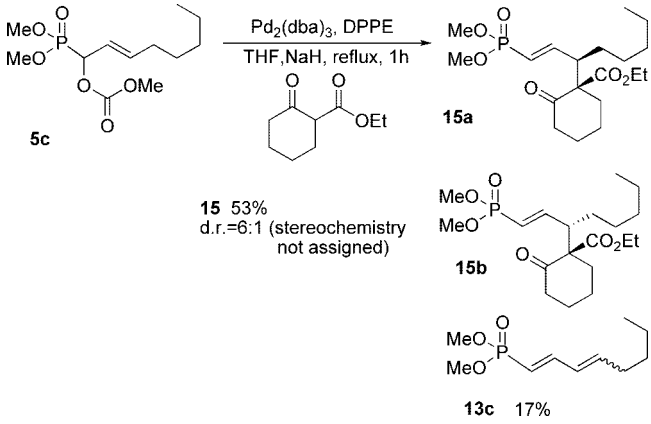
TABLE 2. Palladium-Catalyzed Intermolecular Nucleophilic Substitution



Entry	compound	R	% e.e **5**	% Yield **1** (% e.e)
1	**b**	Ph	71	97 (71)
2	**c**	n-C_5H_{11}	92	56 (92)
3	**e**	$CH_2CH(CH_3)_2$	90	79 (90)
4	**f**	c-C_6H_{11}	95	70 (95)
5	**g**		70% (d.r.) 90%(d.r.)	70% (d.r.)[a] 90% (d.r.)

[a] Determined by ^{31}P NMR spectroscopy.

SCHEME 7. Addition of Ethyl 2-Cyclohexanone Carboxylate

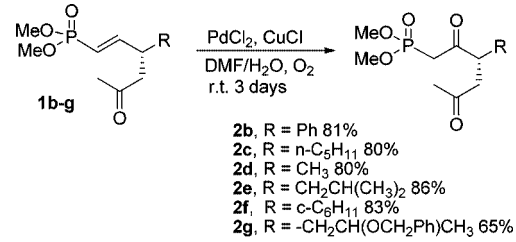


by HPLC, reflected the enantiomeric ratio of the starting phophono carbonate **5**, again demonstrating that the reaction is stereospecific. Unfortunately, the diastereomers **1g** could not be separated by HPLC. However, each diastereomer showed a unique signal in the ^{31}P NMR spectrum and therefore the ratio could be determined by integration.

In general, the intermolecular allylic substitution gave much better yields than the intramolecular decarboxylative rearrangement. For example, when R = Ph and $CH_2CH(Me)_2$, the intermolecular substitution gave the vinyl phosphonate **1** in 97% and 79% yield, respectively (Table 2, entries 1 and 3), whereas the intramolecular decarboxylative rearrangement gave the vinyl phosphonates **1** in 56% and 35% yield, respectively (Table 1, entries 1 and 4). However, in the formation of vinyl phosphonate **1c**, the intermolecular substitution and intermolecular rearrangement gave a similar result (56% and 61% yield, respectively).

To further examine the nucleophilic substitution, a more sterically hindered nucleophile was examined (Scheme 7). Reaction of the phosphono allylic carbonate **5c** with ethyl

SCHEME 8. Wacker Oxidation of Vinyl Phosphonates

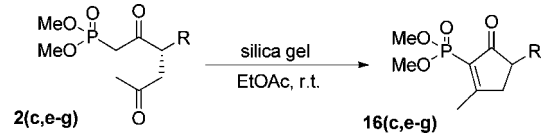


2-cyclohexanone carboxylate in the presence of $Pd_2(dba)_3$, dppe and NaH in THF solution afforded vinyl phosphonate **15** in 53% isolated yield as a 6:1 mixture of diastereoisomers. However, in this case, formation of the diene **13c** (17%) accompanied the substitution reaction.

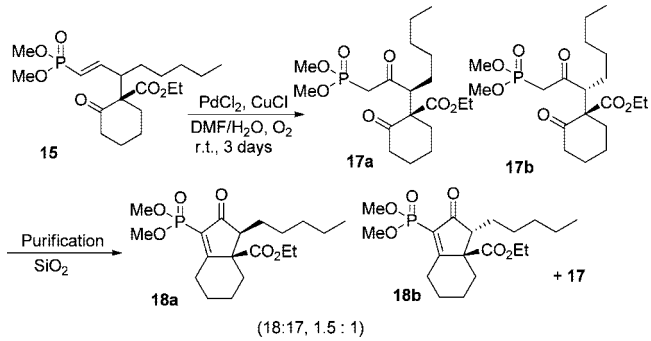
Treatment of vinyl phosphonates **1** with $PdCl_2$, CuCl in DMF, and H_2O under 1 atm of oxygen yielded corresponding ω,β-diketophosphonates **2** (Scheme 8). It was found that pretreating the solution of $PdCl_2$ and CuCl in DMF and H_2O with O_2 for half an hour before the addition of the vinyl phosphonate **1** gave better results.

The Wacker oxidation is slow and usually takes 3 days at room temperature to go to completion. However, the reaction is clean with high regioselectivity and no other products are observed. The yields are generally very good (**2b**−**f**, 80−86%). Oxidation of the vinyl phosphonate **1g** was unique and gave the diketophosphonate **2g** in a lower 65% yield. This may be due to the small electron-withdrawing effect of the benzyloxy propyl group, which reduces the reactivity of alkene. Unfortunately, the diketophosphonates **2** would not separate on any of the several chiral stationary phases examined. However, it is probable that the Wacker oxidation would not result in any detectable levels of racemization. This fact was supported by analysis of the NMR spectra (^1H, ^{13}C, ^{31}P) of **2g**, which showed the same diastereomer ratios as the starting vinyl phosphonate **1g**.

SCHEME 9. The Intramolecular Aldol Reaction of Diketophosphonates



SCHEME 10. Wacker Oxidation and Aldol Condensation



The diketophosphonates **2** are sensitive to silica gel and during prolonged column chromatography an aldol reaction takes place to give the α-phosphonato-α,β-unsaturated cyclopentenones **16** (Scheme 9). The rate of formation of aldol product varies greatly depending on the substituents. No aldol products were observed after the chromatographic purification of diketophosphonates **2b** and **2d** (R = Ph and Me). However, chromatographic purification of diketophosphonates **2c**, **2e**, **2f**, and **2g** always resulted in some formation of the aldol product **16**.

The role of SiO_2 in formation of aldol products **16** was verified by stirring diketophosphonates **2** in EtOAc over silica gel and monitoring the reaction progress by ^{31}P NMR spectroscopy. α-Phosphonato-α,β-unsaturated cyclopentenones **16** are very attractive synthetic intermediates and similar structures were reported earlier by Oh and co-workers.[19] However, it appears that the α-phosphonato-α,β-unsaturated cyclopentenones **16** racemize under the mildly acidic conditions in which they form. The SiO_2-catalyzed aldol reaction of the diketophosphonates **2c** (>90% ee) gave the corresponding cyclopentenone **16c** with <60% ee (Scheme 9). Indeed, the stereochemistry of a sample stored in chloroform continued to erode.

The Wacker oxidation of the more hindered vinyl phosphonate **15** proceeded smoothly to afford diketophosphonate **17**. Again, a mixture of expected keto product **17** (^{31}P = 23 ppm) and the aldol product α-phosphonato-α,β-unsaturated cyclopentenone **18** (^{31}P = 14 ppm) with a 1:1.5 ratio was observed after column chromatography (Scheme 10).

The Intramolecular Horner−Wadsworth−Emmons (HWE) Reaction. The intramolecular HWE results in the formation of carbocycles (and heterocycles) and has been applied to the preparation of rings of various sizes. There have been several sets of reaction conditions reported for both the intra- and the intermolecular HWE reaction.[3,20] The choice of base for the intramolecular HWE reaction of diketophosphonates **2** proved to be critical. Commonly used reaction conditions for intermolecular HWE reactions (e.g., DBU/LiCl) failed to give the desired products. Some of the stronger bases (e.g., NaH in DME) gave cyclopentenone in low isolated yield (<10%). Fortunately, treatment of the diketophosphonates **2** with K_2CO_3 and 18-crown-6 in THF at 40 °C provided cyclopentenones **3** in yields ranging from 77% to 91% (Table 3, entries 1, 2, and 4). Cyclization of the diketophosphonate **2d** gave the cyclopentenone **3d** in a somewhat lower yield (63%), probably because the product was volatile.

Unfortunately, when nonracemic diketophosphonates **2** were used in the HWE reaction, the cyclopentenones were obtained with variable levels of racemization. When phosphonates **2c** and **2e** with 92% and 88% ee, respectively, (Table 3 entries 2 and 6), were subjected to the HWE reaction, the cyclopentenones **3c** and **3e** were isolated with 75% and 69% ee, respectively. Reaction of the phosphonate **2b** (Table 3, entry 1) always gave the corresponding cyclopentenone as a racemic mixture. The enolate is conjugated to the aromatic ring (Scheme 11) and is therefore more stable and forms easily.

Roush and Masamune reported that the combination of K_2CO_3 and 18-C-6 is capable of racemizing chiral centers next to a ketone in the HWE.[21] They also observed that a silyloxy group ($OSiMe_2t$-Bu) at the δ-position was eliminated when using K_2CO_3 as the base. Whereas, DBU/LiCl avoided the problem of elimination, these conditions failed to cyclize the diketophosphonates **2**.

The biphase system reported by Heathcock for intramolecular HWE reactions was also investigated.[3j,k] Treatment of the ketophosphonates **2c** (65% ee) and **2e** (83% ee) with 0.85 equiv of 40 wt % of $Bu_4N^+ {}^-OH$ in H_2O solution in toluene provided products **3c** and **3e** in 60% and 42% isolated yield and with a reduced 44% and 67% ee, respectively (Table 3, entries 4 and 7). Aldol products **16** were isolated and showed considerable racemization of chiral center. Lithium hydroxide (Table 3 entry 10) gave similar results.

Paterson reported that $Ba(OH)_2$ can be used as a base for sensitive substrates in the intermolecular HWE reaction.[22] Aldehydes and ketophosphonates bearing chiral centers α to the carbonyl group, or with silyloxy groups ($OSiMe_2t$-Bu) which were prone to elimination, underwent HWE reaction smoothly to yield the desired products without racemization, epimerization, or elimination.

Treatment of diketophosphonate **2** with 0.8−0.95 equiv of $Ba(OH)_2$ in THF at room temperature gave the desired cyclopentenones **3** with competitive formation of α-phosphonato-α,β-unsaturated cyclopentenones **16** (Table 3, entries 2, 8, 11,

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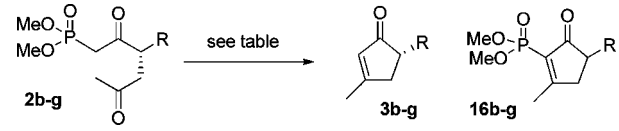
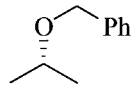
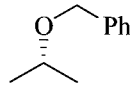
(20) (a) Rübsam, F.; Evers, A. M.; Michel, C.; Giannis, A. *Tetrahedron* **1997**, *53*, 1707. (b) Heathcock, C. H.; Hadley, C. R.; Rosen, T.; Theisen, P. D.; Hecker, S. J. *J. Med. Chem.* **1987**, *30*, 1858. (c) Heathcock, C. H.; Rosen, T. *J. Am. Chem. Soc.* **1985**, *107*, 3731. (d) Astles, P. C.; Thomas, E. J. *J. Chem. Soc., Perkin Trans. 1* **1997**, 845. (e) Roush, W. R.; Warmus, J. S.; Works, A. B. *Tetrahedron Lett.* **1993**, *34*, 4427. (f) Marshall, J. A.; DuBay, W. J. *J. Org. Chem.* **1994**, *59*, 1703. (g) Mulzer, J.; Berger, M. *Tetrahedron Lett.* **1998**, *39*, 803. (h) Bonadies, F.; Cardilli, A.; Lattanzi, A.; Orelli, L. R.; Scettri, A. *Tetrahedron Lett.* **1994**, *35*, 3383. (i) Blackwell, C. M.; Davidson, A. H.; Launchbury, S. B.; Lewis, C. N.; Morrice, E. M.; Reeve, M. M.; Roffey, J. A. R.; Tipping, A. S.; Todd, R. S. *J. Org. Chem.* **1992**, *57*, 1935. (j) Rathke, M. W.; Nowak, M. *J. Org. Chem.* **1985**, *50*, 2624. (k) Yamanoi, T.; Akiyama, T.; Ishida, E.; Abe, K.; Amemiya, M.; Inazu, T. *Chem. Lett.* **1989**, 335. (l) Kann, N.; Rein, T. *J. Org. Chem.* **1993**, *58*, 3802. (m) Kiefel, M. J.; Maddock, J.; Pattenden, G. *Tetrahedron Lett.* **1992**, *33*, 3227.

(21) Blanchette, M. A.; Choy, W.; Davis, J. T.; Essenfeld, A. P.; Masamune, S.; Roush, W. R.; Sakai, T. *Tetrahedron Lett.* **1984**, *25*, 2183.

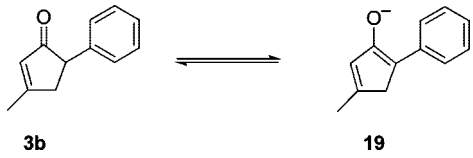
(22) (a) Paterson, I.; Yeung, K.-S.; Smaill, J. B. *Synlett* **1993**, 774. (b) Paterson, I.; Yeung, K.-S.; Watson, C.; Ward, R. A.; Wallace, P. A. *Tetrahedron* **1998**, *54*, 11935. (c) Paterson, I.; Wallace, D. J. *Tetrahedron Lett.* **1994**, *35*, 9477. (d) Ibarra, C. A.; Arias, S.; Fernández, M. J.; Sinisterra, J. V. *J. Chem. Soc., Perkin Trans. II* **1989**, 503. (e) Lafontaine, J. A.; Porvencal, D. P.; Gardelli, C.; Leahy, J. W. *J. Org. Chem.* **2003**, *68*, 4215. (f) Ghosh, A. K.; Gong, G. *J. Am. Chem. Soc.* **2004**, *126*, 3704. (g) Bach, J.; Berenguer, R.; Garcia, J.; Vilarrasa, J. *Tetrahedron Lett.* **1995**, *36*, 3425. (h) Hulme, A. N.; Howells, G. E.; Walker, R. H. *Synlett* **1998**, 828.

TABLE 3. The Intramolecular Horner−Wadsworth−Emmons (HWE) Reaction



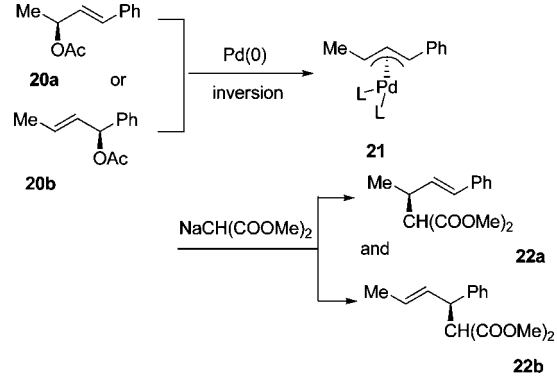
Entry	Compound	R	% e.e. **4**	Conditions	Yield **16** (%.e.e)	% Yield **3** (% e.e.)
1	**b**	Ph	71	K_2CO_3, 18-C-6 THF, 40 °C	---	77 (±)
2	**b**	Ph		0.8-0.95 eq. $Ba(OH)_2$, THF, r.t.	ND	21 (±)
3	**c**	n-C_5H_{11}	>92	K_2CO_3, 18-C-6 THF, 40 °C	---	91 (75)
4	**c**	n-C_5H_{11}	65	0.85 eq. Bu_4N^+ ^-OH PhMe, H_2O, r.t.	13	60 (44)
5	**d**	Me	70	K_2CO_3, 18-C-6 THF, 40 °C	---	63 (~70)
6	**e**	$CH_2CH(CH_3)_2$	88	K_2CO_3, 18-C-6 THF, 40 °C	---	88 (69)
7	**e**	$CH_2CH(CH_3)_2$	83	0.85 eq. Bu_4N^+ ^-OH PhMe, H_2O, r.t.	38	42 (67)
8	**e**	$CH_2CH(CH_3)_2$	88	0.8-0.95 eq. $Ba(OH)_2$ THF, r.t.	11 (58)	23 (86)
9	**e**	$CH_2CH(CH_3)_2$	85	6 eq. $Ba(OH)_2$ THF, r.t.	11 (22)	20 (82)
10	**e**	$CH_2CH(CH_3)_2$	85	0.9 eq. LiOH THF, r.t.	25 (±)	23 (70)
11	**f**	c-C_6H_{11}-	95	0.8-0.95 eq. $Ba(OH)_2$ THF, r.t.	ND	31 (93)
12	**g**		90 (d.e.)	0.8-0.95 eq. $Ba(OH)_2$, THF, r.t.	54 (42)	36 (90)
13	**g**		90 (d.e.)	6.0 eq. $Ba(OH)_2$ THF, r.t.	50 (80)	17 (77)

SCHEME 11. Facile Racemization of Cyclopentenone 3b



and 12). It appears that when using $Ba(OH)_2$ as base, the cyclopentenones were formed with no erosion in the stereochemistry. For example, diketophosphonate **2e** [R = $CH_2CH(Me)_2$] in 88% ee gave the cyclopentenone **3e** with >85% ee (Table 3, entry 8). Similarly, diketophosphonate **2f** (95% ee) and **2g** (90% de) gave cyclopentenones **3f** and **3g** without loss of stereochemistry (95% ee and 90% de, respectively, Table 3 entries 11 and 12). However, cyclization of diketophosphonate **2b** again gave racemic cyclopentenone **3b** (Table 3, entry 2). Unfortunately, in all cases the yields of the cyclopentenone are quite low, ranging from 21% to 36%, mainly due to competitive formation of the aldol products **16**. Using a larger excess of $Ba(OH)_2$ did not help improve the yields of the cyclopentenone and resulted in more racemization (Table 3, entries 9 and 13).

SCHEME 12. Stereochemistry of the Palladium-Catalyzed Intermolecular Nucleophilic Substitution

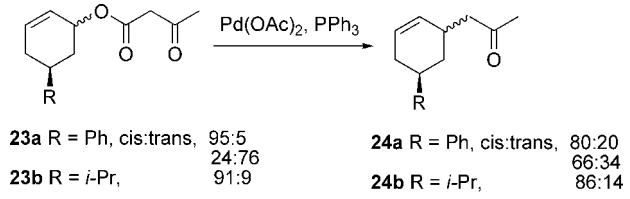


Discussion

The palladium-catalyzed intermolecular substitution reaction of soft nucleophiles with allylic acetates and carbonates has been extensively studied.[23] It is generally accepted that the allylic system **20** reacts with palladium(0) to form the π-allylpalladium complex **21** with inversion of configuration (Scheme 12). Nucleophilic attack on the π-allylpalladium complex also

(23) (a) Trost, B. M.; Crawley, M. L. *Chem. Rev.* **2003**, *103*, 2921, and references cited therein. (b) Wills, M. *Chem. Soc. Rev.* **1995**, 177, and references cited therein. (c) Prat, M.; Ribas, J.; Moreno-Maòas, M. *Tetrahedron* **1992**, *48*, 1695. (d) Byström, S. E.; Aslanian, R.; Bäckvall, J.-E. *Tetrahedron Lett.* **1985**, *26*, 1749. (e) Hayashi, T.; Yamamoto, A.; Hagihara, T. *J. Org. Chem.* **1986**, *51*, 723. (f) Tsuji, Y.; Kusui, T.; Kojima, T.; Sugiura, Y.; Yamada, N.; Tanaka, S.; Ebihara, M. l.; Kawamura, T. *Organometallics* **1998**, *17*, 4835.

SCHEME 13. The Fiaud Study



proceeds with inversion of configuration to give the products **22** with overall retention (Scheme 12). The regiochemistry is generally driven by the steric and electronic biases in the π-allylpalladium complex. The addition of nucleophiles to phosphonate-substituted π-allylpalladium complexes, unlike all-carbon substituted π-allylpalladium complexes, is highly regioselective.

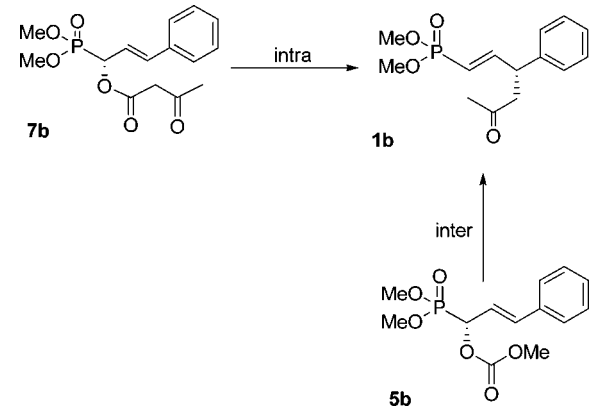
The decarboxylative rearrangement of allylic acetoacetates (Carroll rearrangement) can be somewhat more complex. Fiaud and co-workers investigated the stereochemical outcome of the palladium-catalyzed Carroll rearrangement[24] using the now standard substituted cyclohexenol substrates (Scheme 13). When the substituent is a phenyl group **23a** with a cis/trans ratio of 95/5, a product **24a** with a cis/trans ratio of 80/20 is recovered. This result is mirrored with the isopropyl substituent **23b** with a cis/trans ratio of 91/9, which gives the product **24b** with a cis/trans ratio of 86/14. However, when the substituent is a phenyl group and predominant in the trans isomer (cis/trans ratio 24/76), the product is formed with a cis/trans ratio of 66/34. It was concluded that when the substituent and acetoacetate are cis to each other (diequatorial), the major reaction pathway is stereospecific and goes with retention of configuration. However, when the substituent and the acetoacetate are trans to each other (axial−equatorial), other factors come into play and the major reaction pathway results in a loss of stereochemistry. The loss of the selectivity was attributed to the palladium-assisted epimerization of the starting acetoacetates **23a**,**b**.

Although the cyclohexyl derivatives have been used to probe the stereochemistry of π-allylpalladium-mediated reactions, the presence of the additional stereocenter can have undue influence on the stereochemical outcome of the reaction. It is better to observe the reaction on a nonracemic compound in the absence of additional chiral centers. A comparison of the HPLC data of the vinyl phosphonates **1b** derived from the inter- and intramolecular reactions (Scheme 14) and originating from the same hydroxy phosphonate **4b** sample showed that products were identical in absolute configuration and ee. Since it is generally assumed that the intermolecular nucleophilic substitution takes place with retention of configuration, it can be concluded that the intramolecular rearrangement also proceeds with retention of configuration

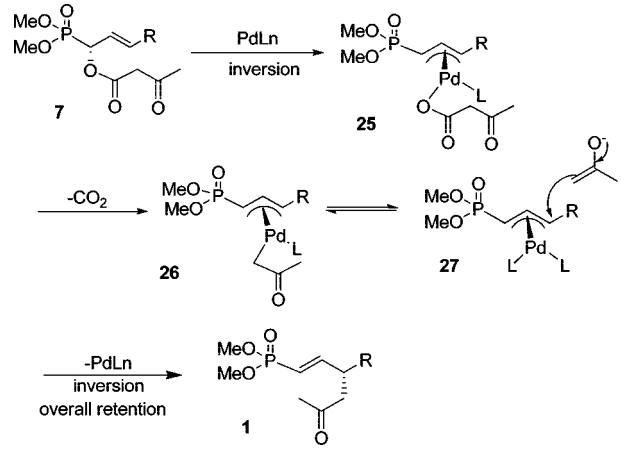
A reasonable mechanistic rationale for the stereochemistry observed in decarboxylative rearrangement of allylic acetoacetates is provided in Scheme 15.[24] Oxidative addition of palladium to the allylic phosphonate **7** proceeds with inversion of configuration to form the π-allylpalladium complex **25**. Decarboxylation of π-allylpalladium **25** yields the intermediate **26**, which can potentially react in two different ways. Direct reductive elimination would yield the vinyl phosphonate with overall inversion of configuration. However, it is proposed that

(24) (a) Fiaud, J. C.; Aribi-Zouioueche, L. *Tetrahedron Lett.* **1982**, *23*, 5279. (b) Bäckvall, J.-E.; Nordberg, R. E.; Vågberg, J. *Tetrahedron Lett.* **1983**, *24*, 411.

SCHEME 14. A Comparison of the Stereochemical Outcome in the Inter- and Intramolecular reactions



SCHEME 15. Proposed Mechanism for the Rearrangement

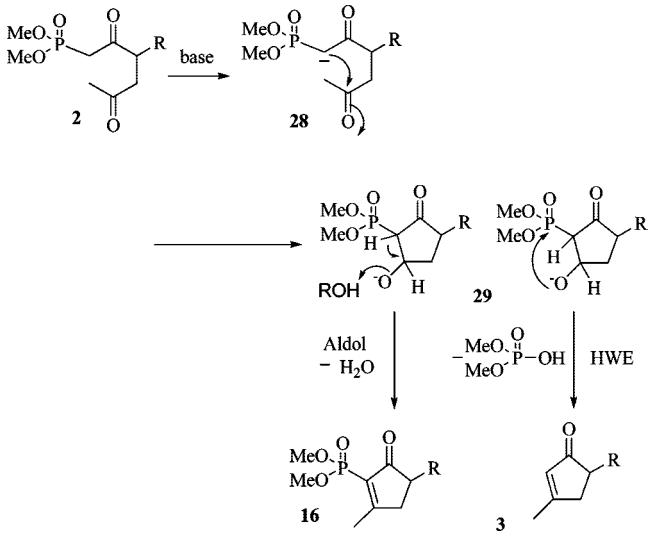


the enolate disassociates from the palladium and attacks the back face of the π-allylpalladium complex **27** affording the vinyl phosphonate **2** with overall retention.

The competitive formation of cyclopentenones **3** and α-phosphonato-α,β-unsaturated cyclopentenones **16** under basic conditions appears to be a function of the base used in the reaction. Under mildly acidic conditions (SiO_2), the aldol reaction is dominant. Under basic conditions, the diketophosphonates **2** will be deprotonated to form anionic intermediate **28** (Scheme 16). Nucleophilic attack of anion to the carbonyl group will give the cyclopentanone intermediates **29**, which can react in two different ways. The desired HWE reaction appears to be favored with the more nucleophilic potassium alkoxide (K_2CO_3, 18-crown-6). However, these reaction conditions also promote racemization. Alternatively, under milder, nonracemizing conditions [$Ba(OH)_2$], the elimination of H_2O to form α-phosphonato-α,β-unsaturated cyclopentenones **16** becomes competitive.

In summary, we have demonstrated that palladium-catalyzed reactions of phosphono carbonates and acetoacetates proceed with complete transfer of chirality. The two-step intermolecular nucleophilic substitution/decarboxylation protocol gave the vinyl phosphonates in higher overall yield. The Wacker oxidation of vinyl phosphonates provided diketophosphonates in good chemical yields with high regioselectivity. β-Ketophosphonates were prone to aldol reaction to form α-phosphonato-α,β-unsaturated cyclopentenones. β,ω-Diketophosphonates readily underwent the intramolecular HWE reaction with K_2CO_3 and 18-C-6 as base affording cyclopentenones with high chemical

SCHEME 16. Formation of Cyclopentenones and α-Phosphonato-α,β-unsaturated Cyclopentenones



yields, but with significant erosion of the stereochemistry. The application $Ba(OH)_2$ as base gave cyclopentenones without racemization, but in generally low (21−36%) yields due to competitive formation of α-phosphonato-α,β-unsaturated cyclopentenones.

Experimental Section

(*R*)-Dimethyl [1-Hydroxy-2-octenyl]phosphonate, 4c[10a]. Hydroxy phosphonate **4b** (0.50 g, 2.1 mmol), 1-heptene (1.7 mL, 12 mmol), and Grubbs second generation catalyst (0.088 g, 0.10 mmol) in CH_2Cl_2 (6 mL) were heated for 24 h at 40 °C. Evaporation of the solvent and column chromatography (SiO_2, hexane:EtOAc, 3:1) gave the pure product **4c** as a colorless oil (0.32 g, 66%). ^{1}H NMR ($CDCl_3$) δ 5.88 (1H, m), 5.59 (1H, m), 4.45 (1H, dd, J_{HH} = 7.1 Hz, J_{HP} = 10.4 Hz), 3.80 (3H, d, J_{HP} = 10.4 Hz), 3.79 (3H, d, J_{HP} = 10.4 Hz), 2.08 (2H, m), 1.31 (6H, m), 0.87 (3H, t, J_{HH} = 6.6 Hz); ^{13}C NMR ($CDCl_3$) δ 135.8 (d, $^3J_{CP}$ = 13.2 Hz), 124.2 (d, $^2J_{CP}$ = 3.7 Hz), 69.4 (d, $^1J_{CP}$ = 160.8 Hz), 53.8 (d, $^2J_{CP}$ = 5.1 Hz), 53.7 (d, $^2J_{CP}$ = 5.3 Hz), 32.5 (d, $^4J_{CP}$ = 1.3 Hz), 31.5, 28.8 (d, $^5J_{CP}$ = 2.7 Hz), 22.7, 14.2; ^{31}P{^{1}H} NMR ($CDCl_3$) δ 25.1.

(*R*)-Dimethyl [1-Hydroxy-3-cyclohexyl-2-propenyl]phosphonate, 4f. Hydroxy phosphonate **4b** (0.50 g, 2.1 mmol), vinyl cyclohexane (2.0 mL, 14 mmol), and Grubbs second generation catalyst (0.088 g, 0.10 mmol) in CH_2Cl_2 (6 mL) were heated for 24 h at 40 °C. Evaporation of the solvent and column chromatography (SiO_2, hexane:EtOAc, 3:1) gave the pure product **4f** as a colorless oil (0.34 g, 66%). IR (neat, NaCl) 3300 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 5.78 (1H, m), 5.49 (1H, m), 4.38 (1H, dd, J_{HH} = 10.3 Hz, J_{HP} = 7.1 Hz), 3.74 (3H, d, J_{HP} = 10.4 Hz), 3.73 (3H, d, J_{HP} = 10.4 Hz), 2.79 (1H, broad), 1.96 (1H, m), 1.65 (4H, m), 0.76−1.26 (6H, m); ^{13}C NMR ($CDCl_3$) δ 141.5 (d, $^3J_{CP}$ = 12.9 Hz), 121.7 (d, $^2J_{CP}$ = 3.8 Hz), 69.6 (d, $^1J_{CP}$ = 160.3 Hz), 53.9 (d, $^2J_{CP}$ = 6.1 Hz), 53.8 (d, $^2J_{CP}$ = 6.8 Hz), 40.9 (d, $^4J_{CP}$ = 1.4 Hz), 32.8 (d, $^5J_{CP}$ = 2.5 Hz), 32.7 (d, $^5J_{CP}$ = 2.3 Hz), 26.3, 26.1; ^{31}P{^{1}H} NMR ($CDCl_3$) δ 25.0; HRMS (EI, M$^+$) calcd for $C_{11}H_{21}O_4P$ 248.1177, found 248.1173.

Dimethyl [1-(Methoxycarbonyloxy)-3-cyclohexanyl-2-propenyl]phosphonate, 5f. Phosphono carbonate **5a** (0.676 g, 3.02 mmol), vinyl cyclohexane (2.50 mL, 18.2 mmol), and Grubbs second generation catalyst (0.128 g, 0.151 mmol) in CH_2Cl_2 (10 mL) were heated for 24 h at 40 °C. Evaporation of the solvent and column chromatography (SiO_2, hexane:EtOAc, 3:1) gave the pure product **5f** as a pale yellow oil (0.82 g, 74%). IR (neat, NaCl) 1755 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 5.93 (1H, m), 5.52 (2H, m), 3.82 (3H, s), 3.81 (3H, d, J_{HP} = 10.6 Hz), 3.80 (3H, d, J_{HP} = 10.7 Hz), 2.02 (1H, m), 1.64−1.75 (4H, m), 1.04−1.33 (6H, m); ^{13}C NMR ($CDCl_3$) δ 154.9 (d, $^3J_{CP}$ = 9.4 Hz), 144.3 (d, $^3J_{CP}$ = 12.2 Hz), 118.1 (d, $^2J_{CP}$ = 3.6 Hz), 73.4 (d, $^1J_{CP}$ = 169.7 Hz), 55.5, 54.1 (d, $^2J_{CP}$ = 6.9 Hz), 53.9 (d, $^2J_{CP}$ = 6.5 Hz), 40.6, 32.5 (d, $^5J_{CP}$ = 2.1 Hz), 32.3 (d, $^5J_{CP}$ = 2.0 Hz), 26.2, 26.0; ^{31}P{^{1}H} NMR ($CDCl_3$) δ 20.3; HRMS (EI, M$^+$) calcd for $C_{13}H_{23}O_6P$ 306.1232, found 306.1235.

Dimethyl [1-(Methoxycarbonyloxy)-5-benzyloxy-2-hexenyl]-phosphonate, 5g. Phosphono carbonate **5a** (1.0 g, 4.6 mmol), 2-benzyloxy-4-pentene (1.83 g, 9.16 mmol), and Grubbs second generation catalyst (0.194 g, 0.229 mmol) in CH_2Cl_2 (10 mL) were heated for 24 h at 40 °C. Evaporation of the solvent and column chromatography (SiO_2, hexane:EtOAc, 3:1) gave the **5g** (mixture of diastereomers) as a pale yellow oil (1.5 g, 90%). IR (neat, NaCl) 1755 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.29 (5H, m), 6.00 (1H, m), 5.65 (1H, m), 5.47 (1H, dd, J_{HH} = 7.7 Hz, J_{HP} = 12.9 Hz), 4.52 (2H, m), 3.81 (9H, m), 3.61 (1H, m), 2.43 (1H, m), 2.32 (1H, m), 1.20 (1.5 H, d, J_{HH} = 6.2 Hz), 1.19 (1.5H, d, J_{HH} = 6.2 Hz); ^{13}C NMR ($CDCl_3$) δ 155.0, 154.9, 138.9, 134.9 (d, $^3J_{CP}$ = 12.5 Hz), 134.8 (d, $^3J_{CP}$ = 12.5 Hz), 128.6, 127.8, 127.7, 127.6, 122.9 (d, $^2J_{CP}$ = 3.2 Hz), 122.8 (d, $^2J_{CP}$ = 3.6 Hz), 74.3, 74.2, 73.1 (d, $^1J_{CP}$ = 170.6 Hz), 73.0 (d, $^1J_{CP}$ = 169.9 Hz), 70.7, 55.6, 54.0 (d, $^2J_{CP}$ = 7.6 Hz), 53.5 (d, $^2J_{CP}$ = 7.1 Hz), 39.7, 39.6, 19.7; ^{31}P{^{1}H} NMR ($CDCl_3$) δ 20.2 and 20.3; HRMS (FAB, MH$^+$) calcd for $C_{17}H_{26}O_7P$ 373.1416, found 373.1419.

General Procedure for the Preparation of Acetoacetates 7 from Hydroxy Phosphonates 4. Diketene (0.30 mL, 4.15 mmol) was added to a solution of hydroxy phosphonate **4** (3.19 mmol) in THF (5 mL) and CH_2Cl_2 (5 mL) at −20 °C, followed by addition of DMAP (0.009 g, 0.0013 mmol). The reaction mixture was stirred at −20 °C for 30 min. The mixture was allowed to warm to room temperature, and then it was stirred overnight. The reaction mixture was washed with 0.1% NaOH (twice) and the aqueous layer was re-extracted with CH_2Cl_2. The combined organic layers were dried over anhydrous $MgSO_4$ and the solvent was evaporated in vacuo. The crude product was purified by chromatography (SiO_2, hexane: EtOAc, 1:1) to give the acetoacetate **7** as pale yellow oil (usually ∼86% keto and ∼14% enol) and the dienes **13**.

Dimethyl [1-(2-Ketobutanoyloxy)-3-phenyl-2-propenyl]phosphonate, 7b. Diketene (0.85 mL, 11 mmol) was added to hydroxy phosphonate **4b** (2.34 g, 9.68 mmol) in THF (15 mL) and CH_2Cl_2 (15 mL) at −20 °C, followed by addition of DMAP (0.005 g, 0.04 mmol). The product **7b** was obtained as pale yellow oil (2.57 g, 81%). IR (neat, NaCl) 1752, 1750 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.16 (5H, m), 6.65 (1H, dd, J_{HP} = 3.9 Hz, J_{HH} = 15.9 Hz,), 6.09 (1H, m), 5.75 (1H, ddd, J_{HH} = 7.5, 0.8 Hz, J_{HP} = 13.7 Hz), 3.67 (3H, d, J_{HP} = 10.7 Hz), 3.65 (3H, d, J_{HP} = 10.7 Hz), 3.43 (2H, s), 2.13 (3H, s); ^{13}C NMR ($CDCl_3$) δ 199.7, 165.6 (d, $^3J_{CP}$ = 7.9 Hz), 135.9 (d, $^3J_{CP}$ = 12.6 Hz), 135.5 (d, $^4J_{CP}$ = 2.2 Hz), 128.7, 128.6, 126.9 (d, $^5J_{CP}$ = 1.4 Hz), 119.2 (d, $^2J_{CP}$ = 4.7 Hz), 69.9 (d, $^1J_{CP}$ = 170.4 Hz), 53.9 (d, $^2J_{CP}$ = 7.0 Hz), 53.8 (d, $^2J_{CP}$ = 6.5 Hz), 49.9, 30.2; ^{31}P{^{1}H} NMR ($CDCl_3$) δ 21.2 (enol), 20.7 (keto); HRMS (CI, MH$^+$) calcd for $C_{15}H_{20}O_6P$ 327.0998, found 327.0992.

Dimethyl [1-(2-Ketobutanoyloxy)-2-octenyl]phosphonate, 7c. Diketene (0.85 mL, 11 mmol) was added to a solution of hydroxy phosphonate **4c** (1.99 g, 8.45 mmol) in THF (12 mL) and CH_2Cl_2 (12 mL) at −20 °C, followed by addition of DMAP (0.004 g, 0.034 mmol). The product **7c** was obtained as a pale yellow oil (2.4 g, 91%). IR (neat, NaCl) 1753, 1721 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 5.94 (1H, m), 5.70 (1H, ddd, J_{HH} = 7.8, 0.7 Hz, J_{HP} = 12.4 Hz), 5.56 (1H, m), 3.81 (3H, d, J_{HP} = 10.9 Hz), 3.79 (3H, d, J_{HP} = 10.7 Hz), 3.53 (2H, s), 2.29 (3H, s), 2.09 (2H, m), 1.33 (6H, m), 0.89 (3H, t, J_{HH} = 6.6 Hz); ^{13}C NMR ($CDCl_3$) δ 199.8, 165.7 (d, $^3J_{CP}$ = 7.8 Hz), 139.5 (d, $^3J_{CP}$ = 12.5 Hz), 120.2 (d, $^2J_{CP}$ = 4.0 Hz), 70.1 (d, $^1J_{CP}$ = 170 Hz), 53.9 (d, $^2J_{CP}$ = 5.4 Hz), 53.8 (d, $^2J_{CP}$ = 4.7 Hz), 50.1, 32.6 (d, $^4J_{CP}$ = 1.0 Hz), 31.5, 30.3, 28.5 (d, $^5J_{CP}$ = 2.6 Hz), 22.6, 14.2; ^{31}P{^{1}H} NMR ($CDCl_3$) δ 21.4 (enol), 20.9 (keto); HRMS (EI, M$^+$) calcd for $C_{14}H_{25}O_6P$ 320.1389, found 320.1381.

Dimethyl [1-(2-Ketobutanoyloxy)-2-butenyl]phosphonate, 7d. Diketene (1.1 mL, 14 mmol) was added to a solution of hydroxy phosphonate **4d** (1.92 g, 10.7 mmol) in THF (14 mL) and CH_2Cl_2 (14 mL) at −20 °C, followed by addition of DMAP (0.005 g, 0.043 mmol). The product **7d** was obtained as a pale yellow oil (2.53 g, 90%). IR (neat, NaCl) 1751, 1719 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.95 (1H, m), 5.65 (1H, m), 5.54 (1H, m), 3.78 (3H, d, J_{HP} = 10.7 Hz), 3.76 (3H, d, J_{HP} = 10.7 Hz), 3.51 (2H, s), 2.25 (3H, s), 1.74 (3H, m); ^{13}C NMR ($CDCl_3$) δ 199.9, 165.7 (d, $^3J_{CP}$ = 7.9 Hz), 134.2 (d, $^3J_{CP}$ = 12.8 Hz), 121.5 (d, $^2J_{CP}$ = 4.1 Hz), 69.8 (d, $^1J_{CP}$ = 171 Hz), 53.9 (d, $^2J_{CP}$ = 6.7 Hz), 53.8 (d, $^2J_{CP}$ = 6.1 Hz), 49.9, 30.2, 18.2 (d, $^4J_{CP}$ = 1.1 Hz); $^{31}P\{^1H\}$ NMR ($CDCl_3$) δ 21.4 (enol), 20.9 (keto); HRMS (EI, M^+) calcd for $C_{10}H_{17}O_6P$ 264.0763, found 264.0757.

General Procedure for the Intramolecular Rearrangement of Phosphono Acetoacetates 7. $Pd(OAc)_2$ (0.134 g, 0.598 mmol) and PPh_3 (0.627 g, 2.39 mmol) were stirred together in anhydrous THF (15 mL) for 5 min at room tempertaure. A solution of phosphono acetoacetate **7** (11.9 mmol) in THF (5 mL) was added. The reaction flask was placed in a preheated oil bath and heated at 70 °C for 1 h. The reaction mixture was allowed to cool, and then it was partitioned between brine and Et_2O. After separation, the aqueous layer was re-extracted with Et_2O and the combined organic layers were dried over anhydrous $MgSO_4$. The solvent was evaporated in vacuo to give the crude product, which was purified by chromatography (SiO_2, EtOAc:hexanes, 3:1) to give the product **1**.

General Procedure for the Intermolecular Allylic Substitution of Phosphono Allylic Carbonates 5 with *tert*-Butyl Acetoacetate. $Pd_2(dba)_3$ (0.044 g, 0.048 mmol) and dppe (0.058 g, 0.14 mmol) were stirred together in anhydrous THF (7 mL) for 5 min. at room temperature. *tert*-Butyl acetoacetate (0.32 mL, 1.9 mmol) was added, followed by a solution of phosphono carbonate **5** (0.968 mmol) in anhydrous THF (2 mL). The reaction flask was placed in a preheated oil bath and heated at 75 °C for 1 h. The reaction mixture was allowed to cool, and then the solvent was evaporated in vacuo to give the crude product. The crude product was redissolved in anhydrous toluene (4 mL) and then trifluoroacetic acid (1.5 mL) was added. The reaction flask was placed in a preheated oil bath and heated at 80 °C for 1 h. The reaction mixture was allowed to cool and then it was diluted with CH_2Cl_2 and washed with saturated aqueous Na_2CO_3. After separation, the aqueous layer was re-extracted with CH_2Cl_2 and the combined organic layers were dried over anhydrous $MgSO_4$. The solvent was evaporated in vacuo to give the crude product, which was purified by chromatography (SiO_2, EtOAc:hexanes, 3:1) to provide the vinyl phosphonate **1**.

Dimethyl [3-(2-Ketopropyl)-3-phenyl-1-propenyl]phosphonate, 1b. Intramolecular Rearrangement. To a solution of $Pd(OAc)_2$ (0.134 g, 0.598 mmol) and PPh_3 (0.627 g, 2.39 mmol) in anhydrous THF (15 mL) was added a solution of phosphono acetoacetate **7b** (3.90 g, 11.9 mmol) in THF (5 mL) to give the product **1b** as pale yellow oil (1.87 g, 56%). IR (neat, NaCl) 1714 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.96 (5H, m), 6.64 (1H, ddd, J_{HH} = 17.2, 6.5 Hz, J_{HP} = 23.6 Hz), 5.28 (1H, ddd, J_{HH} = 17.3, 1.3 Hz, J_{HP} = 19.3 Hz), 3.81 (1H, m), 3.41 (3H, d, J_{HP} = 11.1 Hz), 3.39 (3H, d, J_{HP} = 11.1 Hz), 2.67 (2H, dd, J_{HH} = 7.3 Hz, J_{HP} = 1.4 Hz), 1.82 (3H, s); ^{13}C NMR ($CDCl_3$) δ 206.0, 155.3 (d, $^2J_{CP}$ = 5.1 Hz), 140.4 (d, $^4J_{CP}$ = 0.8 Hz), 128.8, 127.7, 127.1, 116.1 (d $^1J_{CP}$ = 186 Hz), 52.2 (d, $^2J_{CP}$ = 5.5 Hz), 48.3, 44.4 (d, $^3J_{CP}$ = 21.6 Hz), 29.9; $^{31}P\{^1H\}$ NMR ($CDCl_3$) δ 22.3; HRMS (CI, MH^+) calcd for $C_{14}H_{20}O_4P$ 283.1099, found 283.1097.

Intermolecular Allylic Substitution. To a solution of $Pd_2(dba)_3$ (0.044 g, 0.048 mmol) and dppe (0.058 g, 0.145 mmol) in anhydrous THF (7 mL) was added *tert*-butyl acetoacetate (0.32 mL, 1.9 mmol) and phosphono carbonate **5b** (0.29 g, 0.97 mmol) in anhydrous THF (2 mL) to give, after treatment with toluene and TFA, the product **1b** as a pale yellow oil (0.26 g, 97%) spectroscopically identical with the products described above.

Dimethyl [3-(2-Ketopropyl)-1-octenyl]phosphonate, 1c. Intramolecular Rearrangement. To a solution of $Pd_2(dba)_3$ (0.016 g, 0.018 mmol) and dppe (0.021 g, 0.053 mmol) in anhydrous THF (5 mL) was added phosphono acetotoacetate **7c** (0.112 g, 0.350 mmol) in THF (2 mL) to give the product **1c** as pale yellow oil (0.059 g, 61% yield). IR (neat, NaCl) 1716 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.58 (1H, ddd, J_{HH} = 17.2, 8.4 Hz, J_{HP} = 25.6 Hz), 5.59 (1H, ddd, J_{HH} = 17.2, 1.0 Hz, J_{HP} = 20.5 Hz), 3.68 (3H, d, J_{HP} = 11.1 Hz), 3.67 (3H, d, J_{HP} = 11.1 Hz), 2.75 (1H, m), 2.49 (2H, m), 1.98 (3H, s), 1.32 (6H, m), 0.84 (3H, t, J_{HH} = 6.5 Hz); ^{13}C NMR ($CDCl_3$) δ 206.7, 157.0 (d, $^2J_{CP}$ = 4.3 Hz), 115.9 (d, $^1J_{CP}$ = 186 Hz), 52.4 (d, $^2J_{CP}$ = 5.6 Hz), 52.3 (d, $^2J_{CP}$ = 5.6 Hz), 47.9, 39.6 (d, $^3J_{CP}$ = 21.2 Hz), 33.9, 31.8, 30.7, 26.8, 22.6, 14.1; $^{31}P\{^1H\}$ NMR ($CDCl_3$) δ 21.5; HRMS (EI, MH^+) calcd for $C_{13}H_{26}O_4P$ 277.1569, found 277.1580. Anal. Calcd for $C_{13}H_{25}O_4P \cdot {}^1/_4H_2O$: C, 55.61; H, 9.09; O, 24.24. Found: C, 56.40; H, 9.25; O, 24.49.

Dimethyl [(1*E*),(3*E*)-Octadienyl]phosphonate, 13ca. ^1H NMR ($CDCl_3$) δ 6.94 (2H, m), 6.03 (1H, m), 5.37 (1H, m), 3.73 (3H, d, J_{HP} = 11.2 Hz), 2.20 (2H, q, J_{HH} = 6.7 Hz), 1.39 (4H, m), 0.90 (3H, t, J_{HH} = 7.1 Hz) ppm; ^{13}C NMR ($CDCl_3$) δ 150.2 (d, $^2J_{CP}$ = 3.7 Hz), 145.7 (d, $^4J_{CP}$ = 2.2 Hz), 127.5 (d, $^3J_{CP}$ = 9.5 Hz), 111.0 (d, $^1J_{CP}$ = 183 Hz), 52.3 (d, $^2J_{CP}$ = 5.5 Hz), 32.8, 31.1, 22.5, 14.1; $^{31}P\{^1H\}$ NMR ($CDCl_3$) δ 21.0.

Dimethyl [(1*E*),(3*Z*)-Octadienyl]phosphonate, 13cb. ^1H NMR ($CDCl_3$) δ 7.09 (1H, ddd, J_{HH} = 16.9, 9.7 Hz, J_{HP} = 26.6 Hz), 6.13 (2H, m), 5.53 (1H, dd, J_{HH} = 16.9 Hz, J_{HP} = 19.7 Hz), 3.72 (6H, d, J_{HP} = 11.1 Hz), 2.16 (2H, q, J_{HH} = 6.0 Hz), 1.38 (4H, m), 0.91 (3H, t, J_{HH} = 7.0 Hz); ^{13}C NMR ($CDCl_3$) δ 150.6 (d, $^2J_{CP}$ = 6.1 Hz), 144.9, 129.6 (d, $^3J_{CP}$ = 26.5 Hz), 113.1 (d, $^1J_{CP}$ = 191 Hz), 52.7 (d, $^2J_{CP}$ = 5.5 Hz), 32.9, 31.2, 22.6, 14.2; $^{31}P\{^1H\}$ NMR ($CDCl_3$) δ 23.2.

Intermolecular Allylic Substitution. To a solution of $Pd_2(dba)_3$ (0.050 g, 0.055 mmol) and dppe (0.066 g, 0.16 mmol) in THF were added *tert*-butyl acetoacetate (0.36 mL, 2.2 mmol) and phosphono carbonate **5c** (0.32 g, 1.1 mmol) to give, after treatment with toluene and TFA, the product **1c** as a pale yellow oil (0.17 g, 56%).

Dimethyl [3-(2-Ketopropyl)-1-butenyl]phosphonate, 1d. Intramolecular Rearrangement. A solution of $Pd(PPh_3)_4$ (0.361 g, 0.313 mmol) and phosphono acetoactetae **7d** (2.17 g, 8.21 mmol) in anhydrous THF (35 mL) gave the product **1d** as a pale yellow oil (1.27 g, 71%). IR (neat, NaCl) 1710 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.71 (1H, ddd, J_{HH} = 17.3, 6.7 Hz, J_{HP} = 23.9 Hz), 5.59 (1H, ddd, J_{HH} = 17.3, 1.4 Hz, J_{HP} = 20.1 Hz), 3.69 (3H, d, J_{HP} = 11.1 Hz), 3.68 (3H, d, J_{HP} = 11.1 Hz), 2.88 (1H, m), 2.49 (2H, m), 2.11 (3H, s), 1.05 (2H, d, J_{HH} = 6.8 Hz); ^{13}C NMR ($CDCl_3$) δ 206.6, 157.9 (d, $^2J_{CP}$ = 4.4 Hz), 114.4 (d, $^1J_{CP}$ = 187 Hz), 52.5 (d, $^2J_{CP}$ = 5.6 Hz), 49.1 (d, $^5J_{CP}$ = 1.0 Hz), 33.5 (d, $^3J_{CP}$ = 21.5 Hz), 30.6, 18.9 (d, $^4J_{CP}$ = 0.8 Hz); $^{31}P\{^1H\}$ NMR ($CDCl_3$) δ 21.7; HRMS (EI, MH^+) calcd for $C_9H_{18}O_4P$ 221.0943, found 221.0934.

Dimethyl [(1*E*),(3*E*)-Butadienyl]phosphonate, 13d. ^1H NMR ($CDCl_3$) δ 7.08 (1H, m), 6.43 (1H, m), 5.64 (3H, m), 3.74 (3H, d, J_{HP} = 11.1 Hz), 3.72 (3H, J_{HP} = 11.1 Hz); ^{13}C NMR ($CDCl_3$) δ 150.1 (d, $^2J_{CP}$ = 5.9 Hz), 136.0 (d, $^3J_{CP}$ = 26.8 Hz), 116.9 (d, $^1J_{CP}$ = 190 Hz), 52.8 (d, $^2J_{CP}$ = 5.6 Hz); $^{31}P\{^1H\}$ NMR ($CDCl_3$) δ 22.2; HRMS (EI, M^+) calcd for $C_6H_{11}O_3P$ 162.0446, found 162.0443.

Dimethyl [3-(2-Ketopropyl)-5-methyl-1-hexenyl]phosphonate, 1e. Intramolecular Rearrangement. To a solution of $Pd_2(dba)_3$ (0.106 g, 0.116 mmol) and dppe (0.139 g, 0.349 mmol) in anhydrous THF (40 mL) was added a solution of phosphono actoacetate **7e** (0.711 g, 2.32 mmol) in THF (5 mL) to give the product **1e** as a pale yellow oil (0.324 g, 35%). IR (neat, NaCl) 1715 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.58 (1H, ddd, J_{HH} = 17.2, 8.7 Hz, J_{HP} = 25.8 Hz), 5.62 (1H, dd, J_{HH} = 17.2 Hz, J_{HP} = 20.6 Hz), 3.70 (3H, d, J_{HP} = 11.1 Hz), 3.69 (3H, d, J_{HP} = 11.1 Hz), 2.87 (1H, m), 2.49 (2H, d, J_{HH} = 6.7 Hz), 2.11 (3H, s), 1.53 (1H, m), 1.24 (2H, m), 0.88 (3H, d, J_{HH} = 6.5 Hz), 0.87 (3H, d, J_{HH} = 6.6 Hz); ^{13}C NMR ($CDCl^3$) δ 206.6, 157.1 (d, $^2J_{CP}$ = 2.8 Hz), 116.0 (d, $^1J_{CP}$ = 186 Hz), 52.5 (d, $^2J_{CP}$ = 5.6 Hz), 52.4 (d, $^2J_{CP}$ = 5.6 Hz), 48.4, 43.3, 37.7 (d, $^3J_{CP}$ = 21.2 Hz), 30.8, 25.7, 23.4, 21.8;

$^{31}P\{^1H\}$ NMR ($CDCl_3$) δ 21.3; HRMS (EI, M^+) calcd for $C_{12}H_{23}O_4P$ 262.1334, found 262.1336. Anal. Calcd for $C_{12}H_{23}O_4P\cdot^1/_4H_2O$: C, 54.03; H, 8.82; O, 25.52. Found: C, 53.76; H, 8.77; O, 25.77.

Dimethyl [(1*E*)(3*E*)-5-Methylhexadienyl]phosphonate, 13ea. ^1H NMR ($CDCl_3$) δ 6.89 (2H, m), 5.96 (1H, m), 5.35 (1H, dd, J_{HH} = 11.7 Hz, J_{HP} = 17.2 Hz), 3.71 (6H, d, J_{HP} = 11.2 Hz), 2.45 (1H, m), 1.03 (6H, d, J_{HH} = 6.8 Hz); ^{13}C NMR ($CDCl_3$) δ 152.2 (d, $^4J_{CP}$ = 2.3 Hz), 150.4 (d, $^2J_{CP}$ = 5.7 Hz), 124.7 (d, $^3J_{CP}$ = 9.5 Hz), 111.2 (d, $^1J_{CP}$ = 184 Hz), 52.2 (d, $^2J_{CP}$ = 5.4 Hz), 31.7, 22.1; $^{31}P\{^1H\}$ NMR ($CDCl_3$) δ 20.9.

Dimethyl [(1*E*)(3*Z*)-5-Methylhexadienyl]phosphonate, 13ed. ^1H NMR ($CDCl_3$) δ 7.09 (1H, m), 6.08 (2H, m), 5.55 (1H, dd, J_{HH} = 16.9 Hz, J_{HP} = 19.7 Hz), 3.71 (6H, d, J_{HP} = 11.1 Hz), 2.40 (1H, m), 1.03 (6H, d, J_{HH} = 6.8 Hz); ^{13}C NMR ($CDCl_3$) δ 151.1, 150.6 (d, $^2J_{CP}$ = 6.0 Hz), 126.6 (d, $^3J_{CP}$ = 26.7 Hz), 113.2 (d, $^1J_{CP}$ = 191 Hz), 52.5 (d, $^2J_{CP}$ = 5.5 Hz), 31.5, 21.9; $^{31}P\{^1H\}$ NMR ($CDCl_3$) δ 23.3.

Intermolecular Allylic Substitution. To a solution of $Pd_2(dba)_3$ (0.153 g, 0.167 mmol) and dppe (0.199 g, 0.499 mmol) in anhydrous THF (22 mL) was added *tert*-butyl acetoacetate (1.1 mL, 6.7 mmol) and phosphono carbonate **5e** (0.977 g, 3.49 mmol) in anhydrous THF (5 mL) to give, after treatment with toluene and TFA, the product **1e** as a pale yellow oil (0.69 g, 79%).

Dimethyl [3-(2-Ketopropyl)-3-cyclohexyl-1-propenyl]phosphonate, 1f. Intermolecular Allylic Substitution. To a solution of $Pd_2(dba)_3$ (0.019 g, 0.021 mmol) and dppe (0.025 g, 0.062 mmol) in THF were added *tert*-butyl acetoacetate (0.20 mL, 1.2 mmol) and the phosphono carbonate **5f** (0.180 g, 0.589 mmol) in THF (8 mL) to give, after treatment with toluene and TFA, the product **1f** as a pale yellow oil (0.12 g, 70%). IR (neat, NaCl) 1715 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.62 (1H, ddd, J_{HH} = 8.7 Hz, J_{HH} = 17.2 Hz, J_{HP} = 25.9 Hz), 5.58 (1H, ddd, J_{HH} = 0.8 Hz, J_{HH} = 17.2 Hz, J_{HP} = 20.9 Hz), 3.70 (3H, d, J_{HP} = 11.1 Hz), 3.69 (3H, d, J_{HP} = 11.1 Hz), 2.59 (2H, m), 2.12 (3H, s), 1.69 (6H, m), 0.88−1.40 (6H, m); ^{13}C NMR ($CDCl_3$) δ 207.1, 155.9, (d, $^2J_{CP}$ = 4.4 Hz), 116.9 (d, $^1J_{CP}$ = 185 Hz), 52.5 (d, $^2J_{CP}$ = 5.6 Hz), 52.4 (d, $^2J_{CP}$ = 5.6 Hz), 45.3 (d, $^3J_{CP}$ = 20.9 Hz), 45.2, 41.3, 30.9, 30.8, 30.1, 26.6, 26.5; $^{31}P\{^1H\}$ NMR ($CDCl_3$) δ 21.7; HRMS (EI, M^+) calcd for $C_{14}H_{25}O_4P$ 288.1490, found 288.1491. Anal. Calcd for $C_{14}H_{25}O_4P\cdot^1/_2\ H_2O$: C, 56.57; H, 8.75. Found: C, 56.62; H, 8.57.

Dimethyl [3-(2-Ketopropyl)-5-(*R*)-benzyloxyl-1-propenyl]phosphonate, 1g. Intermolecular Allylic Substitution. To a solution of $Pd_2(dba)_3$ (0.139 g, 0.152 mmol) and ddpe (0.182 g, 0.456 mmol) in THF were added *tert*-butyl acetoacetate (1.26 mL, 7.60 mmol) and phosphonate carbonate **5g** (1.41 g, 3.80 mmol) in anhydrous THF (27 mL total) to give, after treatment with toluene and TFA, the product (1:1 mixture of diastereoisomers) **1g** as a pale yellow oil (0.94 g, 70%). IR (neat, NaCl) 1715 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.34 (5H, m), 6.61 (1H, m), 5.56 (1H, m), 4.58 (1H, dd, J_{HH} = 11.5, 9.5 Hz), 4.35 (1H, dd, J_{HH} = 19.4, 11.5 Hz), 3.66 (6H, m), 3.48 (1H, m), 3.01 (1H, m), 2.49 (2H, m), 2.06 (3H, d, J_{HH} = 8.2 Hz), 1.69 (1H, m), 1.47 (1H, m), 1.21 (1.5H, d, J_{HH} = 6.2 Hz), 1.19 (1.5H, d, J_{HH} = 6.5 Hz); ^{13}C NMR ($CDCl_3$) δ 206.5, 206.4, 156.8 (d, $^2J_{CP}$ = 4.4 Hz), 156.6 (d, $^2J_{CP}$ = 4.2 Hz), 138.8, 138.7, 128.6, 128.5, 128.0, 127.9, 127.8, 116.7 (d, $^1J_{CP}$ = 185 Hz), 115.7 (d, $^1J_{CP}$ = 186 Hz), 72.5, 72.1, 70.5, 70.3, 52.5 (d, $^2J_{CP}$ = 5.3 Hz), 52.5 (d, $^2J_{CP}$ = 5.3 Hz), 52.44 (d, $^2J_{CP}$ = 5.5 Hz), 52.40 (d, $^2J_{CP}$ = 5.4 Hz), 48.6, 47.3, 41.7, 40.8, 36.8 (d, $^3J_{CP}$ = 21.7 Hz), 36.2 (d, $^3J_{CP}$ = 21.5 Hz), 30.6, 30.5, 19.9, 19.6; $^{31}P\{^1H\}$ NMR ($CDCl_3$) δ 21.7 and 21.6; HRMS (EI, MH^+) calcd for $C_{18}H_{28}O_5P$ 355.1674, found 355.1679. Anal. Calcd for $C_{18}H_{27}O_5P\cdot^1/_2H_2O$: C, 59.50; H, 7.71; O, 24.24. Found: C, 59.78; H, 7.67; O, 24.03.

Dimethyl [3-(1-Ethoxycarbonyl-2-ketocyclohexyl)-1-octenyl]phosphonate, 15. A solution of $Pd_2(dba)_3$ (0.019 g, 0.020 mmol) and dppe (0.024 g, 0.060 mmol) in anhydrous THF (3 mL) was stirred at room temperature for 5 min, then a solution of NaH (0.021 g, 0.052 mmol), ethyl 2-cyclohexanone carboxylate (0.10 mL 0.60 mmol), and phosphono carbonate **5c** (0.119 g, 0.403 mmol) in anhydrous THF (5 mL) was added. The reaction flask was placed in a preheated oil bath and heated at 75 °C for 1 h. The reaction mixture was allowed to cool and then it was washed with 5% HCl until the solution was neutral. After separation, the aqueous layer was re-extracted with CH_2Cl_2 and the combined organic layers were dried over anhydrous $MgSO_4$. The solvent was evaporated in vacuo to give the crude product, which was purified by chromatography (SiO_2, EtOAc:hexanes, 1:5) to give **15** as a pale yellow oil (0.083 g, 53%) (mixture of diastereomers). IR (neat, NaCl) 1713 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.53 (1H, J_{HH} = 17.1, 10.3 Hz, J_{HP} = 27.3 Hz), 5.58 (1H, dd, J_{HH} = 17.1 Hz, J_{HP} = 21.3 Hz), 4.17 (2H, q, J_{HH} = 7.1 Hz), 3.71 (3H, d, J_{HP} = 11.0 Hz), 3.70 (3H, d, J_{HP} = 11.0 Hz), 2.79 (1H, m), 2.40 (3H, m), 1.97 (1H, m), 1.67 (4H, m), 1.29 (11H, m), 0.88 (3H, t, J_{HH} = 7.4 Hz); ^{13}C NMR ($CDCl_3$) δ 205.9, 170.7, 153.2 (d, $^2J_{CP}$ = 4.6 Hz), 119.0 (d, $^1J_{CP}$ = 184.4 Hz), 64.7, 61.7, 52.5 (d, $^2J_{CP}$ = 5.1 Hz), 52.4 (d, $^2J_{CP}$ = 5.5 Hz), 49.1 (d, $^3J_{CP}$ = 21.6 Hz), 41.8, 31.8, 31.7, 29.7, 27.9, 26.9, 22.7, 22.6, 14.3, 14.2; $^{31}P\{^1H\}$ NMR ($CDCl_3$) δ 20.7; HRMS (EI, MH^+) calcd for $C_{19}H_{33}O_6P$ 389.2093, found 389.2091.

General Procedure for the Wacker Oxidation. $PdCl_2$ (0.052 g, 0.29 mmol) and CuCl (0.145 g, 1.46 mmol) were dissolved in H_2O (1 mL) and DMF (1.4 mL). The reaction mixture was stirred under O_2 (1 atm) for 0.5 h at room temperature, then a solution of vinyl phosphonate **1** (1.46 mmol) in DMF (1 mL) was added. The reaction was stirred for 3 days at room temperature, then the reaction was diluted with CH_2Cl_2 and washed with saturated aqueous NH_4Cl (2×). After separation, the aqueous layer was re-extracted with CH_2Cl_2 and the combined organic layers were dried over anhydrous $MgSO_4$. The solvent was evaporated in vacuo to give the crude product, which was purified by chromatography (SiO_2, EtOAc: hexanes 3:1) to give the product **2**. Prolonged residence on the column also gave the phsophono cyclopentenones **16**.

Dimethyl [3-(2-Ketopropyl)-2-keto-3-phenylpropyl]phosphonate, 2b. $PdCl_2$ (0.052 g, 0.29 mmol), CuCl (0.145 g, 1.46 mmol), and vinyl phosphonate **1b** (0.412 g, 1.46 mmol) were stirred in H_2O (1 mL) and DMF (2.4 mL) under O_2 (1 atm) to give **2b** as a pale yellow oil (0.352 g, 81%). IR (neat, NaCl) 1706 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.36 (5H, m), 4.49 (1H, dd, J_{HH} = 9.6, 4.3 Hz), 3.84 (3H, d, J_{HP} = 11.2 Hz), 3.75 (3H, d, J_{HP} = 11.3 Hz), 3.46 (1H, dd, J_{HH} = 17.9, 9.6 Hz), 3.24 (1H, J_{HH} = 14.8 Hz, J_{HP} = 22.3 Hz), 3.03 (1H, J_{HH} = 14.8 Hz, J_{HP} = 21.3 Hz), 2.69 (1H, J_{HH} = 17.9, 4.3 Hz), 2.23 (3H, s); ^{13}C NMR ($CDCl_3$) δ 206.2, 200.7 (d, $^2J_{CP}$ = 6.1 Hz), 137.1, 129.5, 128.7, 128.1, 54.5 (d, $^3J_{CP}$ = 3.2 Hz), 53.2 (d, $^2J_{CP}$ = 6.5 Hz), 53.1 (d, $^2J_{CP}$ = 6.3 Hz), 46.5, 39.7 (d, $^1J_{CP}$ = 133 Hz), 30.1; $^{31}P\{^1H\}$ NMR ($CDCl_3$) δ 23.6; HRMS (CI, MH^+) calcd for $C_{14}H_{20}O_5P$ 299.1040, found 299.1048.

Dimethyl [3-(2-Ketopropyl)-2-ketooctyl]phosphonate, 2c. $PdCl_2$ (0.03 g, 0.169 mmol), CuCl (0.084 g, 0.844 mmol), and vinyl phosphonate **1c** (0.233 g, 0.844 mmol) were stirred in H_2O (1 mL) and DMF (1.4 mL) under O_2 atmosphere to give **2c** as a pale yellow oil (0.197 g, 80%). IR (neat, NaCl) 1711 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.78 (3H, d, J_{HP} = 11.2 Hz), 3.77 (3H, d, J_{HP} = 11.2 Hz), 3.24 (2H, d, J_{HP} = 21.9 Hz), 3.08 (1H, m), 2.92 (1H, ddd, J_{HH} = 17.9, 9.5 Hz, J_{HP} = 1.7 Hz), 2.49 (1H, ddd, J_{HH} = 17.9, 3.9 Hz, J_{HP} = 1.4 Hz), 2.13 (3H, d, J_{HP} = 1.9 Hz), 1.66 (1H, m), 1.38 (1H, m), 1.24 (6H, m), 0.86 (3H, t, J_{HH} = 6.4 Hz); ^{13}C NMR ($CDCl_3$) δ 207.2, 204.8 (d, $^2J_{CP}$ = 6.5 Hz), 53.2 (d, $^2J_{CP}$ = 6.5 Hz), 53.0 (d, $^2J_{CP}$ = 6.4 Hz), 47.7 (d, $^3J_{CP}$ = 3.6 Hz), 44.8, 40.5 (d, $^1J_{CP}$ = 132 Hz), 31.9, 30.7, 29.9, 26.8, 22.6, 14.1; $^{31}P\{^1H\}$ NMR ($CDCl_3$) δ 23.7; HRMS (EI, MH^+) calcd for $C_{13}H_{26}O_5P$ 293.1518, found 293.1514.

Dimethyl [3-(2-Ketopropyl)-2-ketobutyl]phosphonate, 2d. $PdCl_2$ (0.135 g, 0.763 mmol), CuCl (0.382 g, 3.82 mmol), and vinyl phosphonate **1d** (0.840 g, 3.82 mmol) were stirred in H_2O (4 mL) and DMF (6 mL) under O_2 atmosphere to give **2d** as a pale yellow oil (0.717 g, 80%). IR (neat, NaCl) 1709 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.05 (3H, d, J_{HP} = 11.2 Hz), 4.01 (3H, d, J_{HP} = 11.2 Hz), 3.47 (2H, m), 3.20 (1H, dd, J_{HH} = 18.1, 8.8 Hz), 2.72 (1H, dd, J_{HH} = 18.1, 4.5 Hz), 2.37 (3H, s), 1.39 (3H, dd, J_{HH} = 7.2 Hz, J_{HP} = 0.9

Hz); ^{13}C NMR ($CDCl_3$) δ 207.0, 205.1 (d, $^2J_{CP}$ = 6.3 Hz), 53.2 (d, $^2J_{CP}$ = 6.6 Hz), 53.1 (d, $^2J_{CP}$ = 6.5 Hz), 47.1, 42.4 (d, $^3J_{CP}$ = 2.9 Hz), 40.1 (d, $^1J_{CP}$ = 131 Hz), 29.9, 16.4; ^{31}P{^{1}H} NMR ($CDCl_3$) δ 23.5; HRMS (EI, MH^+) calcd for $C_9H_{18}O_5P$ 237.0892, found 237.0899.

Dimethyl [3-(2-Ketopropyl)-2-keto-5-methylhexyl]phosphonate, 2e. $PdCl_2$ (0.113 g, 0.638 mmol), CuCl (0.316 g, 3.19 mmol), and vinyl phosphonate **1e** (0.811 g, 3.10 mmol) were stirred in H_2O (3.5 mL) and DMF (7.5 mL) under O_2 (1 atm) to give **2e** as a pale yellow oil (1.29 g, 86%). IR (neat, NaCl) 1709 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.73 (6H, d, J_{HP} = 11.2 Hz), 3.19 (2H, dd, J_{HH} = 1.3 Hz, J_{HP} = 21.1 Hz), 3.08 (1H, m), 2.84 (1H, dd, J_{HH} = 18.1, 9.6 Hz), 2.46 (1H, dd, J_{HH} = 18.1, 3.8 Hz), 2.08 (3H, s), 1.47 (2H, m), 1.14 (1H, m), 0.87 (3H, d, J_{HH} = 6.3 Hz), 0.83 (3H, d, J_{HH} = 6.0 Hz); ^{13}C NMR ($CDCl_3$) δ 207.3, 205.1 (d, $^2J_{CP}$ = 6.5 Hz), 53.2 (d, $^2J_{CP}$ = 6.4 Hz), 52.9 (d, $^2J_{CP}$ = 6.4 Hz), 45.9 (d, $^3J_{CP}$ = 3.9 Hz), 45.2, 40.4 (d, $^1J_{CP}$ = 133 Hz), 39.7, 29.9, 25.9, 23.2, 21.9; ^{31}P{^{1}H} NMR ($CDCl_3$) δ 23.9; HRMS (EI, MH^+) calcd for $C_{12}H_{24}O_5P$ 279.1361, found 279.1358.

Dimethyl [3-(2-Ketopropyl)-2-keto-3-cyclohexylpropyl]phosphonate, 2f. $PdCl_2$ (0.025 g, 0.14 mmol), CuCl (0.068 g, 0.69 mmol), and vinyl phosphonate **1f** (0.199 g, 0.690 mmol) were stirred in H_2O (1.5 mL) and DMF (3 mL) under O_2 atmosphere to give **2f** as a pale yellow oil (0.173 g, 83%). IR (neat, NaCl) 1709 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.79 (6H, d, J_{HP} = 11.2 Hz), 3.31 (1H, dd, J_{HH} = 15.6 Hz, J_{HP} = 21.9 Hz), 3.24 (1H, dd, J_{HH} = 15.6 Hz, J_{HP} = 21.9 Hz), 3.00 (2H, m), 2.46 (1H, d, J_{HH} = 16.3 Hz), 2.15 (3H, s), 1.48−1.79 (5H, m), 0.83−1.32 (6H, m); ^{13}C NMR ($CDCl_3$) δ 207.6, 204.6 (d, $^2J_{CP}$ = 6.9 Hz), 53.6 (d, $^3J_{CP}$ = 4.8 Hz), 53.3 (d, $^2J_{CP}$ = 6.4 Hz), 52.9 (d, $^2J_{CP}$ = 6.3 Hz), 41.5, 40.9 (d, $^1J_{CP}$ = 135 Hz), 38.8, 31.9, 30.1, 29.2, 26.8, 26.6, 26.3; ^{31}P{^{1}H} NMR ($CDCl_3$) δ 21.7; HRMS (EI, M^+) calcd for $C_{14}H_{25}O_5P$ 304.1439, found 304.1433.

Dimethyl [3-(2-Ketopropyl)-2-keto-5(*R*)-benzoxylhexyl]phosphonate, 2g. $PdCl_2$ (0.0530 g, 0.296 mmol), CuCl (0.147 g, 1.48 mmol), and vinyl phosphonate **1g** (0.524 g, 1.48 mmol) were stirred in H_2O (3.5 mL) and DMF (4.5 mL) under O_2 atmosphere to give **2g** (1:1 mixture of diastereomers) as a pale yellow oil (0.357 g, 65%). IR (neat, NaCl) 1709 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.32 (5H, m), 4.62 (0.5H, d, J_{HH} = 11.7 Hz), 4.51 (0.5H, d, J_{HH} = 11.7 Hz), 4.35 (0.5H, d, J_{HH} = 11.7 Hz), 4.29 (0.5H, d, J_{HH} = 11.7 Hz), 3.75 (6H, m), 3.52 (1H, m), 2.93−3.42 (3.5H, m), 2.83 (0.5H, m), 2.48 (0.5H, dd, J_{HH} = 17.9, 4.8 Hz), 2.35 (0.5H, dd, J_{HH} = 18.2, 4.8 Hz), 2.12 (1.5H, s), 2.08 (1.5H, s), 1.92 (0.5H, m), 1.81 (1H, m), 1.42 (0.5H, m), 1.22 (1.5H, d, J_{HH} = 6.0 Hz), 2.11 (1.5H, d, J_{HH} = 6.0 Hz); ^{13}C NMR ($CDCl_3$) δ 207.02, 207.0, 204.8 (d, $^2J_{CP}$ = 6.5 Hz), 204.4 (d, $^2J_{CP}$ = 6.1 Hz), 138.6, 138.4, 128.6, 128.5, 128.2, 127.9, 72.6, 71.9, 70.6, 70.3, 53.2 (d, $^2J_{CP}$ = 6.2 Hz), 53.1 (d, $^2J_{CP}$ = 6.5 Hz), 53.0 (d, $^2J_{CP}$ = 6.2 Hz), 52.9 (d, $^2J_{CP}$ = 6.4 Hz), 45.1, 44.9 (d, $^3J_{CP}$ = 3.9 Hz), 44.8 (d, $^3J_{CP}$ = 3.4 Hz), 44.7, 40.4 (d, $^1J_{CP}$ = 132 Hz), 40.2 (d, $^1J_{CP}$ = 132 Hz), 38.9, 37.8, 30.1, 29.9, 19.8, 19.7; ^{31}P{^{1}H} NMR ($CDCl_3$) δ 24.3 and 24.1; HRMS (FAB, MH^+) calcd for $C_{18}H_{28}O_6P$ 371.1623, found 371.1626.

(2-Dimethylphosphonato-3-methyl-5-pentyl)-2-cyclopentenone, 16c. IR (neat, NaCl) 1707 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.79 (3H, d, J_{HP} = 11.3 Hz), 3.78 (3H, d, J_{HP} = 11.4 Hz), 2.89 (1H, m), 2.49 (3H, m), 2.41 (2H, m), 1.80 (1H, m), 1.32 (7H, m), 0.88 (3H, t, J_{HH} = 6.5 Hz); ^{13}C NMR ($CDCl_3$) δ 208.0 (d, $^2J_{CP}$ = 11.2 Hz), 190.7 (d, $^2J_{CP}$ = 13.8 Hz), 128.8 (d, $^1J_{CP}$ = 189 Hz), 52.9 (d, $^2J_{CP}$ = 5.9 Hz), 52.8 (d, $^2J_{CP}$ = 5.9 Hz), 46.5 (d, $^3J_{CP}$ = 10.3 Hz), 42.0 (d, $^3J_{CP}$ = 18.1 Hz), 31.9, 31.5, 27.1, 22.7, 20.1 (d, $^3J_{CP}$ = 2.6 Hz), 14.2; ^{31}P{^{1}H} NMR ($CDCl_3$) δ 14.5; HRMS (EI, MH^+) calcd for $C_{13}H_{24}O_4P$ 275.1412, found 275.1414. Anal. Calcd for $C_{13}H_{23}O_4P$: C, 56.93; H, 8.39; O, 23.36. Found: C, 56.54; H, 8.38; O, 23.78.

[2-Dimethylphosphonato-3-methyl-5-(2-methylpropyl)]-2-cyclopentenone, 16e. IR (neat, NaCl) 1708 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.72 (3H, d, J_{HP} = 11.4 Hz), 3.71 (3H, d, J_{HP} = 11.4 Hz), 2.85 (1H, m), 2.42 (3H, m), 2.34 (m), 1.81 (1H, broad), 1.63 (2H, m), 1.13 (1H, m), 0.87 (3H, d, J_{HH} = 6.4 Hz), 0.85 (3H, d, J_{HH} = 6.4 Hz); ^{13}C NMR ($CDCl_3$) δ 208.2 (d, $^2J_{CP}$ = 11.3 Hz), 190.3 (d, $^2J_{CP}$ = 13.8 Hz), 128.7 (d, $^1J_{CP}$ = 189 Hz), 52.9 (d, $^2J_{CP}$ = 5.8 Hz), 44.9 (d, $^3J_{CP}$ = 10.4 Hz), 42.6 (d, $^3J_{CP}$ = 18.2 Hz), 40.7, 26.8, 23.5, 21.9, 20.0 (d, $^3J_{CP}$ = 2.6 Hz); ^{31}P{^{1}H} NMR ($CDCl_3$) δ 14.5; HRMS (EI, MH^+) calcd for $C_{12}H_{22}O_4P$ 261.1256, found 261.1254. Anal. Calcd for $C_{12}H_{21}O_4P \cdot {}^1/_4H_2O$: C, 54.44; H, 8.26. Found: C, 54.21; H, 8.26.

(2-Dimethylphosphonato-3-methyl-5-cyclohexyl)-2-cyclopentenone, 16f. IR (neat, NaCl) 1703 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.79 (3H, d, J_{HP} = 11.4 Hz), 3.77 (3H, d, J_{HP} = 11.4 Hz), 2.74 (1H, m), 2.55 (1H, m), 2.48 (3H, m), 2.42 (1H, m), 1.89 (1H, m), 1.69 (4H, m), 0.93−1.42 (6H, m); ^{13}C NMR ($CDCl_3$) δ 207.9 (d, $^2J_{CP}$ = 11.2 Hz), 191.3 (d, $^2J_{CP}$ = 13.9 Hz), 129.7 (d, $^1J_{CP}$ = 188 Hz), 52.9 (d, $^2J_{CP}$ = 5.9 Hz), 52.8 (d, $^2J_{CP}$ = 5.7 Hz), 51.8 (d, $^3J_{CP}$ = 10.0 Hz), 39.3, 38.6 (d, $^3J_{CP}$ = 18.2 Hz), 31.2, 27.8, 26.6, 26.4, 26.2, 20.0 (d, $^2J_{CP}$ = 2.5 Hz); ^{31}P{^{1}H} NMR ($CDCl_3$) δ 14.4; HRMS (EI, M^+) calcd for $C_{14}H_{23}O_4P$ 286.1334, found 286.1330.

[2-Dimethylphosphonato-3-methyl-5-(2*R*-benzoxylpropyl)]-2-cyclopentenone, 16g. 1:1 mixture of diastereoisomers: IR (neat, NaCl) 1708 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.25 (5H, m), 4.55 (0.5H, d, J_{HH} = 11.8 Hz), 4.51 (0.5H, d, J_{HH} = 11.8 Hz), 4.38 (0.5H, d, J_{HH} = 11.8 Hz), 4.27 (0.5H, d, J_{HH} = 11.8 Hz), 3.72 (6H, m), 3.57 (1H, m), 2.83 (1H, m), 2.61 (1H, m), 2.41 (1H, m), 2.38 (1.5H, m), 2.33 (1.5H, m), 1.91 (1H, m), 1.37 (1H, m), 1.15 (1.5H, d, J_{HH} = 6.0 Hz), 1.15 (1.5H, d, J_{HH} = 6.0 Hz); ^{13}C NMR ($CDCl_3$) δ 207.9 (d, $^2J_{CP}$ = 11.6 Hz), 190.9 (d, $^2J_{CP}$ = 13.8 Hz), 190.7 (d, $^2J_{CP}$ = 13.7 Hz), 138.9, 138.8, 128.7 (d, $^1J_{CP}$ = 184 Hz), 128.5, 128.4 (d, $^1J_{CP}$ = 190 Hz), 128.0, 127.9, 127.8, 74.2, 72.6, 70.8, 70.4, 52.9 (d, $^2J_{CP}$ = 5.7 Hz), 44.1 (d, $^3J_{CP}$ = 10.6 Hz), 43.5 (d, $^3J_{CP}$ = 8.4 Hz), 43.3, 42.4, 42.2, 38.8, 37.9, 20.1, 19.8; ^{31}P{^{1}H} NMR ($CDCl_3$) δ 14.6 and 14.5; HRMS (EI, M^+) calcd for $C_{18}H_{25}O_5P$ 352.1439, found 352.1441.

Genera Procedure for the Horner−Wadsworth−Emmons Cyclization with K_2CO_3 as the Base. Diketophosphonate **2** (0.144 mmol) was dissolved in anhydrous THF (3 mL), then K_2CO_3 (0.040 g, 0.29 mmol) and 18-crown-6 (0.011 g, 0.043 mmol) were added. The reaction flask was placed in a preheated oil bath and heated at 40 °C for 24 h. The reaction mixture was allowed to cool and then it was washed with 5% HCl until the solution was neutral. After separation, the aqueous layer was re-extracted with CH_2Cl_2 and the combined organic layers were dried over anhydrous $MgSO_4$. The solvent was evaporated in vacuo to give the crude product, which was purified by chromatography (SiO_2, EtOAc:hexanes, 1:5) to give the cyclopentenone **3**.

(3-Methyl-5-phenyl)-2-cyclopentenone, 3b. Diketophosphonate **2b** (0.043 g, 0.14 mmol) gave **3b** as a white solid (0.019 g, 77%).

(3-Methyl-5-pentyl)-2-cyclopentenone, 3c. Diketophosphonate **2c** (0.162 g, 0.555 mmol) gave **3c** as a colorless liquid (0.084 g, 91%).

(3,5-Dimethyl)-2-cyclopentenone, 3d. Diketophosphonate **2d** (0.627 g, 2.66 mmol) gave **3d** as a colorless liquid (0.183 g, 63%).

[3-Methyl-5-(2-methylpropyl)]-2-cyclopentenone, 3e. Diketophosphonate **2e** (1.462 g, 5.257 mmol) gave **3e** as a pale yellow oil (0.705 g, 88%).

[3-Methyl-5-(2-benzoxylpropyl)]-2-cyclopentenone, 3g. Diketophosphonate **2g** (0.101 g, 0.272 mmol) gave **3g** as a colorless liquid (0.044 g, 67%).

General Procedure for the Horner−Wadsworth−Emmons Cyclization with $Bu_4N^+OH^-$ as the Base. Diketophosphonate **2** (0.247 mmol) was dissolved in toluene (3 mL) and H_2O (3 mL). Then a 40 wt % $Bu_4N^+OH^-$ solution (0.14 mL, 0.222 mmol) was added. The reaction mixture was stirred vigorously for 1 h at room temperature. The layers were separated and the aqueous layer was re-extracted with Et_2O and the combined organic layers were dried over anhydrous $MgSO_4$. The solvent was evaporated in vacuo to give the crude product, which was purified by chromatography (SiO_2, EtOAc:hexanes, 1:5) to give the products **3** and **16**.

(3-Methyl-5-pentyl)-2-cyclopentenone, 3c. Diketophosphonate **2c** (0.072 g, 0.25 mmol) gave **3c** (0.024 g, 60%).

[3-Methyl-5-(2-methylpropyl)]-2-cyclopentenone, 3e. Diketophosphonate **2e** (0.064 g, 0.23 mmol) gave **3e** (0.015 g, 42%) along with the aldol product **16e** (0.023 g, 38%).

Genera Procedure for the Horner−Wadsworth−Emmons Cyclization with $Ba(OH)_2$ as the Base. Diketophosphonate **2** (0.091 mmol) was dissolved in anhydrous THF (1.2 mL), then $Ba(OH)_2 \cdot 8H_2O$ (dried at 115 °C for 16 h before use, 0.015 g, 0.087 mmol) was added. The reaction mixture was stirred at room temperature until the reaction was complete (TLC). The reaction mixture was partitioned between brine and Et_2O. After separation, the aqueous layer was re-extracted with Et_2O and the combined organic layers were dried over anhydrous $MgSO_4$. The solvent was evaporated in vacuo to give the crude product, which was purified by chromatography (SiO_2, EtOAc:hexanes, 1:5) to give the products **3** and **16**.

(3-Methyl-5-phenyl)-2-cyclopentenone. Diketophosphonate **2b** (0.105 g, 0.352 mmol) gave **3b** as a white solid (0.013 g, 21%).

[3-Methyl-5-(2-methylpropyl)]-2-cyclopentenone, 3e. Diketophosphonate **2e** (0.018 g, 0.065 mmol) gave **3e** (0.002 g, 23%).

(3-Methyl-5-cyclohexyl)-2-cyclopentenone, 3f. Diketophosphonate **2f** (0.028 g, 0.091 mmol) gave **3f** as a pale yellow oil (0.005 g, 31% yield).

[3-Methyl-5-(2-benzoxylpropyl)]-2-cyclopentenone, 3g. Diketophosphonate **2g** (0.085 g, 0.23 mmol) gave **3g** as a pale yellow oil (0.02 g, 36%).

(3-Methyl-5-phenyl)-2-cyclopentenone, 3b. White solid; ^{1}H NMR ($CDCl_3$) δ 7.18 (5H, m), 5.95 (1H, br s), 3.55 (1H, dd, J_{HH} = 7.2, 2.8 Hz), 3.05 (1H, m), 2.61 (1H, m), 2.14 (3H, s); ^{13}C NMR ($CDCl_3$) δ 209.4, 178.3, 140.2, 130.2, 129.2, 127.9, 127.3, 53.1, 43.2, 19.9; HRMS (EI, M^+) calcd for $C_{12}H_{12}O$ 172.0882, found 172.0887.

(3-Methyl-5-pentyl)-2-cyclopentenone, 3c. Colorless liquid; IR (neat, NaCl) 1698 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 5.87 (1H, br s), 2.71 (1H, m), 2.35 (1H, m), 2.23 (1H, m), 2.10 (3H, br s), 1.77 (1H, m), 1.27 (7H, m), 0.86 (3H, t, J_{HH} = 6.7 Hz); ^{13}C NMR ($CDCl_3$) δ 212.4, 177.4, 130.1, 46.9, 39.9, 31.9, 31.5, 27.1, 22.7, 19.5, 14.2; HRMS (EI, MH^+) calcd for $C_{11}H_{19}O$ 167.1436, found 167.1437.

(3,5-Dimethyl)-2-cyclopentenone, 3d. Colorless liquid; IR (neat, NaCl) 1697 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 5.87 (1H, br s), 2.79 (1H, m), 2.39 (1H, m), 2.15 (1H, m), 2.09 (3H, br s), 1.14 (3H, dd, J_{HH} = 7.5, 1.4 Hz); ^{13}C NMR ($CDCl_3$) δ 212.9, 177.2, 129.6, 42.0, 41.3, 19.5, 16.6; HRMS (EI, MH^+) calcd for $C_7H_{10}O$ 110.0732, found 110.0731.

[3-Methyl-5-(2-methylpropyl)]-2-cyclopentenone, 3e. Pale yellow oil; IR (neat, NaCl) 1698 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 5.90 (1H, br s), 2.75 (1H, m), 2.42 (1H, m), 2.23 (1H, m), 2.11 (3H, br s), 1.70 (2H, m), 1.18 (1H, m), 0.93 (3H, d, J_{HH} = 6 Hz), 0.92 (3H, d, J_{HH} = 6 Hz); ^{13}C NMR ($CDCl_3$) δ 212.8, 177.2, 129.9, 45.4, 40.9, 40.6, 26.9, 23.6, 21.9, 19.6.

(3-Methyl-5-cyclohexyl)-2-cyclopentenone, 3f. Pale yellow oil; IR (neat, NaCl) 1698 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 5.89 (1H, br s), 2.56 (1H, m), 2.38 (2H, m), 2.12 (3H, br s), 1.89 (1H, m), 1.70 (4H, m), 0.96−1.43 (6H, m); ^{13}C NMR ($CDCl_3$) δ 212.3, 178.0, 131.1, 52.4, 39.1, 36.3, 31.4, 27.5, 26.7, 26.5, 26.3, 19.6; HRMS (EI, M^+) calcd for $C_{12}H_{18}O$ 178.1358, found 178.1359.

[3-Methyl-5-(2-benzoxylpropyl)]-2-cyclopentenone, 3g. Pale yellow oil (1:1 mixture diastereomers); IR (neat, NaCl) 1696 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.32 (5H, m), 5.82 (1H, br s), 4.61 (0.5H, d, J_{HH} = 11.8 Hz), 4.60 (0.5H, d, J_{HH} = 11.8 Hz), 4.78 (0.5H, d, J_{HH} = 11.8 Hz), 4.39 (0.5H, d, J_{HH} = 11.8 Hz), 3.73 (0.5H, m), 3.59 (0.5H, m), 2.71 (0.5H, m), 2.46 (1.5H, m), 2.26 (1H, m), 2.04 (0.5H, m), 2.03 (1.5H, s), 1.99 (1.5H, s), 1.91 (0.5H, m), 1.47 (0.5H, m), 1.34 (0.5H, m), 1.17 (1.5H, d, J_{HH} = 6.0 Hz), 1.16 (1.5H, d, J_{HH} = 6.0 Hz); ^{13}C NMR ($CDCl_3$) δ 212.3, 212.2, 177.6, 177.5, 139.1, 130.1, 129.8, 128.5, 128.0, 127.9, 127.7, 74.6, 73.0, 70.8, 70.4, 44.6, 43.8, 41.5, 40.4, 39.1, 38.3, 20.1, 19.9, 19.6; HRMS (FAB, MH^+) calcd for $C_{16}H_{21}O_2$ 245.1541, found 245.1537.

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Supporting Information Available: General experimental details, ^{1}H and ^{13}C NMR spectra for compounds **4c**, **4f**, **5b**, **5f**, **5g**, **7b**, **7c**, **7d**, **1b−g**, **13c**, **13e**, **15**, **2b−g**, **3b−g**, **16c**, **16e**, **16f**, and **16 g** and HPLC data for compounds **4b**, **4c**, **5b**, **5f**, **1c**, **1e**, **1f**, **3c**, **3e**, **3f**, **3g**, and **16f**. This material is available free of charge via the Internet at http://pubs.acs.org.

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